09/291656

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File   5:Biosis Previews(R)  1969-2002/Apr W3
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      Set  Items  Description
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Set     Items   Description
S1      14816   LEUKOTRIENE
S2        326   AEROL?
S3          2   S1 AND S2
S4      43223   INHAL?
S5        585   S1 AND S4
S6      26283   INHALATION
S7        262   S1 AND S6
S8          1   LEUKOTRIENE(6W)AEROL?
S9          0   AB=LEUKOTRIENE(3W)INHALATION
S10         0   AB=(LEUKOTRIENE(3W)INHALATION)
S11         7   (LEUKOTRIENE(3W)INHALATION)/AB
S12       176   (LEUKOTRIENE AND INHALATION)/AB
S13         2   (LEUKOTRIENE AND AEROL?)/AB
S14        32   (LEUKOTRIENE AND NEBUL?)/AB
S15        18   S14 NOT S12
? t s3/7/1-2

 3/7/1
DIALOG(R)File   5:Biosis Previews(R)
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08337688   BIOSIS NO.: 000094088936
INHIBITORY EFFECT OF NZ-107 ON ANAPHYLACTIC BRONCHOCONSTRICTION IN
  GUINEA-PIGS AND RATS
AUTHOR: IWAMA T; SHIKADA K-I; YAMAMOTO A; SAKASHITA M; HIBI M; TANAKA S
AUTHOR ADDRESS: SHIRAOKA RES. STN. BIOL. SCI., NISSAN CHEM. INDUSTRIES
  LTD., 1470 SHIRAOKA, SAITAMA 349-02, JPN.
JOURNAL: INT ARCH ALLERGY IMMUNOL 97 (2). 1992. 99-104. 1992
CODEN: IAAIE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We studied the effect of NZ-107 in a number of animal models of
  anaphylactic bronchoconstriction. In conscious guinea pigs, pretreated
  with indomethacin, pyrillamine and propranolol, passively sensitized with
  heterologous anti serum, NZ-107 in doses of 10-30 mg/kg per os inhibited
  the aerosolized antigen-induced cough and collapse. NZ-107 in a high dose
  of 100 mg/kg per os significantly prevented %%%aerolsolized%%%
  antigen-induced anaphylactice collapse, but not cough in actively or
  passively sensitized conscious guinea pigs and also significantly
  protected aerosilized histamine-induced collapse, but not cough in
  conscious collapse, but not cough in guinea pigs. This compound had
  little inhibitory effect on aerosolized acetylcholine-induced cough and
  collapse. In anesthetized animals, the effect of NZ-107 on
  bronchconstriction induced by intravenous administration of antigen and
  various agonists was examined by the method of Konzett and Rossler. In
  doses of 10-50 mg/kg per os, NZ-107 inhibited antigen-induced
  bronchoconstriction in anesthetized guinea pigs. NZ-107 when
  intravenously adminstered to the anesthetized guinea pigs inhibited not
  only %%%leukotriene%%% D4-induced bronchoconstriction, but also
  thromboxane A2 mimetic U-46619-, platelet-activating factor- and
  histamine-induced bronchoconstriction. In anesthetized rats, NZ-107 in a
  dose of 300 mg/kg per os tended to inhiit the antigen-induced
  bronchoconstriction, but this effect was not significant. These results
  indicate that NZ-107 acts as a spasmolytic agent which inhibits bronchial
  responses to antigens or various other bronchoconstrictors in animal
  models, suggesting that NZ-107 may be potentially beneficial in the
  treatment of bronchial asthma.

? t s7/7/145-165

 7/7/145
DIALOG(R)File   5:Biosis Previews(R)
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08296561 BIOSIS NO.: 000094067859
THE EFFECTS OF LIPOXIN A-4 ON AIRWAY RESPONSES IN ASTHMATIC SUBJECTS
AUTHOR: CHRISTIE P E; SPUR B W; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY AND ALLIED RESPIRATORY DISORDERS, 4TH FLOOR, HUNTS' HOUSE, GUY'S HOSP., LONDON SW1 9RT, UK.
JOURNAL: AM REV RESPIR DIS 145 (6). 1992. 1281-1284. 1992
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This study was performed to determine whether lipoxin A4 (LXA4) %%%inhalation%%% in asthmatic subjects has an effect on airways response. Eight subjects (six asthmatic, two normal) attended for bronchial %%%inhalation%%% challenge with LXA4. In three of these subjects (two asthmatics, one normal) blood pressure, pulse, and symptoms before and after challenge were recorded. Subsequently five male patients with mild asthma (22 to 34 yr of age) **reattended for bronchial %%%inhalation%%% challenge with either %%%leukotriene%%% C4 (LTC4)** or the combination of LTC4 and 1 .times. 10-4 M LXA4. After %%%inhalation%%% of each dose of agonist SGaw and V25 were measured. Airway responsiveness was determined by the concentration of agonist in the **nebulizer** required to induce a 35% fall in SGaw (PC35). There was no effect of LXA4 %%%inhalation%%% of SGaw, V25, blood pressure, pulse, or symptoms. There was a significant shift of the SGaw and V25 dose-response curve to the right after %%%inhalation%%% challenge with LTC4 combined with 1 .times. 10-4 M LXA4 as compared with that after %%%inhalation%%% challenge with LTC4 alone ($p < 0.01$ and $p < 0.025$, respectively). Thus, LXA4 may modulate LTC4-induced airway obstruction and may act as an endogenous sulfidopeptide %%%leukotriene%%% receptor antagonist.

7/7/156
DIALOG(R)File 5:Biosis Previews(R)

07911966 BIOSIS NO.: 000093011089
INTERACTION OF THROMBOXANE A2 AND LEUKOTRIENES IN GUINEA-PIG AIRWAYS IN-VIVO
AUTHOR: FUJIMURA M; BANDO T; MIZUHASHI K; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV., SCH. MED., 13-1 TAKARA-MACHI, 920 KANAZAWA, JPN.
JOURNAL: PROSTAGLANDINS 42 (4). 1991. 379-389. 1991
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effects of a thromboxane A2 receptor antagonist (S-1452) on bronchoconstriction induced by **inhaled %%%leukotriene%%% C4** and a %%%leukotriene%%% receptor antagonist (AS-35) on bronchoconstriction caused by %%%inhalation%%% of a thromboxane A2 mimetic (STA2) were studied in anesthetized, artificially ventilated guinea pigs in order to examine the interaction of thromboxane A2 and leukotrienes in airways. 0.01-1.0 .mu. g/ml of %%%leukotriene%%% C4 and 0.1-1.0 .mu. g/ml of STA 2 inhaled from ultrasonic **nebulizer** developed for small animals caused . dose-dependent increase of pressure at the airway opening (Pao) which is considered to be an index representing bronchial response. Pretreatment of the animals with inhaled S-1452 (0.01,0.033 mg/ml) significantly reduced the airway responses produced by 0.01,0.033,0.1,0.33 and 1.0 .mu. g/ml of %%%leukotriene%%% C4 in a dose dependent manner, While pretreatment with inhaled AS-35 (1mg) did not affect the STA2 dose-response curve. These findings suggest that %%%leukotriene%%% C4 activates thromboxane A2 generation while thromboxane A2 does not influence 5-lipoxygenase pathway in the airways.

7/7/157
DIALOG(R)File 5:Biosis Previews(R)

07910042 BIOSIS NO.: 000093009165
INHIBITORY EFFECT OF %%%INHALATION%%% OF A THROMBOXANE SYNTHETASE INHIBITOR ON BRONCHOCONSTRICTION INDUCED BY AEROSOLIZED %%%LEUKOTRIENE%%% C-4 AND THROMBOXANE A-2 ANALOGUE IN ANESTHETIZED GUINEA-PIGS
AUTHOR: FUJIMURA M; OGAWA H; SAITO M; SAKAMOTO S; MIYAKE Y; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA 920, JPN.
JOURNAL: ALLERGY (CPH) 46 (7). 1991. 534-539. 1991
CODEN: LLRGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effect of aerosol administration of a thromboxane synthetase inhibitor (OKY-046) on bronchoconstriction induced by **aerosol %%%leukotriene%%% C4**, histamine and a thromboxane A2 analogue (STA2) was studied in anesthetized, artificially ventilated guinea pigs in order to evaluate the effectiveness of %%%inhalation%%% of OKY-046 on an unfavorable mechanism of secondary release of thromboxane A2. 0.01-1.0 .mu.g/ml %%%leukotriene%%% C4, 25-400 .mu.g/ml histamine and 0.033-1.0 .mu.g/ml STA2 inhaled from an ultrasonic **nebulizer** developed for small animals caused a dose-dependent increase of pressure at the airway opening (Pao), which is considered to be an index representing bronchial response. Pretreatment of the animals with aerosol OKY-046 (0.035 and 0.35 mg/animal) significantly reduced the airway responses produced by %%%inhalation%%% of %%%leukotriene%%% C4 and STA2, in a dose-dependent manner, while the pretreatment did not affect the histamine dose-response curve. These findings suggest that aerosol %%%leukotriene%%% C4 and STA2 activate thromboxane synthesis in the airway, and %%%inhalation%%% of OKY-046 may be useful for preventing the secondary release of thromboxane A2, which is an unfavorable mechanism in asthma.

7/7/158
DIALOG(R)File 5:Biosis Previews(R)

07910028 BIOSIS NO.: 000093009151
THE EFFECT OF INHALED LY-170680 ON %%%LEUKOTRIENE%%% D-4-INDUCED BRONCHOCONSTRICTION IN HEALTHY VOLUNTEERS
AUTHOR: WOOD-BAKER R; PHILLIPS G D; LUCAS R A; TURNER G A; HOLGATE S T
AUTHOR ADDRESS: DEP. RESPIRATORY MED., SIR CHARLES GAIRDNER HOSPITAL, VERDUN STREET, NEDLANDS, PERTH, WESTERN AUSTRALIA 6009, AUST.
JOURNAL: DRUG INVEST 3 (4). 1991. 239-247. 1991
CODEN: DRUIE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The action of inhaled LY-170680 was studied in the airways of healthy men. In the guinea-pig model this drug is a selective %%%leukotriene%%% (LT) antagonist both in vitro and in vivo. The effect of doses between 0.1 and 6 mg on bronchoconstriction induced by **inhaled LTD4** was investigated in a single-blind study. Compared with placebo, LY-170680 2 and 6 mg exerted a protective effect against LTD4 by a rightward shift in the dose-response curve. Two hours after LY-170680 6 mg, the median (range) PD20FEV1 was increased to 24.0 (7.3 to 88.2) nmol from 2.5 (2.8 to 37.1) nmol after placebo. Similarly, 6 hours after LY-170680 2 mg, the median (range) PD40Vp30 was increased to 26.9 (2.3 to 81.4) nmol compared with 3.4 (0.9 to 12.4) nmol after placebo. %%%Inhalation%%% of LY-170680 caused minor cough and throat irritation in some subjects after the 2 and 6 mg doses. It is concluded that LY-170680 administered by %%%inhalation%%% is an effective LTD4 antagonist in healthy human airways and its duration of action is sufficient to suggest that it should be further investigated in asthma.

7/7/160
DIALOG(R)File 5:Biosis Previews(R)

07890994 BIOSIS NO.: 000092140297
A NOVEL METHOD FOR THE EVALUATION OF BRONCHOACTIVE AGENTS IN THE CONSCIOUS

GUINEA-PIG
AUTHOR: BALL D I; COLEMAN R A; HARTLEY R W; NEWBERRY A
AUTHOR ADDRESS: DEP. PERIPHERAL PHARMACOL., GLAXO GROUP RES. LTD., WARE, HERTS. SG12 0DP, UK.
JOURNAL: J PHARMACOL METHODS 26 (3). 1991. 187-202. 1991
FULL JOURNAL NAME: Journal of Pharmacological Methods
CODEN: JPMED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We describe a simple, noninvasive, nontraumatic and reproducible method in which the activities of bronchoactive agents may be recorded in six conscious guinea pigs simultaneously. The method involves the use of "head out" whole body plethysmographs from which respiratory rate can be recorded, by monitoring respiration-related changes in pressure within the body chamber. Exposure of a guinea pig to an aerosolized bronchoconstrictor agent causes an increase in respiratory rate, which is quantified by measuring the area under the respiratory rate curve using a purpose-built respiratory computer. This can be carried out for six animals simultaneously and independently. When exposed to a standard bronchoconstrictor aerosol challenge at intervals over a 6 hr period, the areas under the respiratory rate curves for each animal are highly reproducible. **%%%Inhalation%%% of nebulized solutions** of acetylcholine (ACh), histamine (Hist), 5-hydroxytryptamine, bradykinin, **%%%leukotriene%%% D4** and the thromboxane A2-mimetic, U-46619, but not prostaglandin F2.alpha. (PGF2.alpha.) caused dose-related bronchoconstriction observed as increases in respiratory rate. In addition, salbutamol, clenbuterol, N-ethylcarboxamide adenosine (NECA) and PGE2 all inhibited ACh (1 mg mL-1) and Hist (1 mg mL-1)-induced increases in respiratory rate in a dose-related fashion. The method described, which is both noninvasive and nontraumatic, may therefore be used to quantify in the conscious guinea pig, both bronchoconstrictor and bronchodilator agents.

7/7/162
DIALOG(R)File 5:Biosis Previews(R)

07822846 BIOSIS NO.: 000092104032
THE EFFECT OF %%%INHALATION%%% OF THE %%%LEUKOTRIENE%%% RECEPTOR ANTAGONIST SKF-104353 ON %%%LEUKOTRIENE%%% C-4-INDUCED AND %%%LEUKOTRIENE%%% E-4-INDUCED BRONCHOCONSTRICTION IN SUBJECTS WITH ASTHMA
AUTHOR: CHRISTIE P E; SPUR B W; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY ALLIED RESPIRATORY DISORDERS, 4TH FLOOR, HUNT'S HOUSE, GUY'S HOSPITAL, LONDON SE1 9RT, ENGLAND.
JOURNAL: J ALLERGY CLIN IMMUNOL 88 (2). 1991. 193-198. 1991
FULL JOURNAL NAME: Journal of Allergy and Clinical Immunology
CODEN: JACIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of prior %%%inhalation%%% of the sulfidopeptide %%%leukotriene%%% receptor antagonist, SK&F 104353 (963 .+-. 43.7 .mu.g; mean .+-. SEM), on (LTC4)- and %%%leukotriene%%% E4 (LTE4)-induced bronchoconstriction has been studied in six subjects with asthma (six male subjects, aged 24 to 36 years). **%%%Inhalation%%% challenges with either synthetic LTC4 or LTE4 were performed after** prior %%%inhalation%%% of aerosolized SK&F 104353 or placebo in a double-blind, randomized fashion. Airway responsiveness to each agonist was determined by the cumulative dose of agonist required to induce a 35% fall in specific airway conductance (PD35) as determined by linear interpolation of the log dose-response curve. There was no change in baseline specific airway conductance after %%%inhalation%%% of either placebo or SK&F 104353. LTC4- and LTE4-induced bronchoconstrictions were significantly inhibited by aersolized %%%inhalation%%% of SK&F 104353 30 minutes before challenge. The geometric mean (GM) PD35 of LTC4 on the open-therapy and placebo-therapy days was 0.043 nmol (range, 0.01 to 0.1 nmol) and 0.036 nmol (range, 0.01 to 0.1 nmol), respectively. On the treatment day with SK&F 104353, it was not possible to obtain a GM PD35 LTC4 up to a maximum concentration of 0.52 nmol LTC4 ($p < 0.01$). The GM PD35 of LTE4 on the open-therapy and placebo-therapy days was 0.30 nmol (range, 0.13 to 0.76

nmol) and 0.39 nmol (range, 0.14 to 0.9 nmol), respectively. On the treatment day with SK&F 104353, it was not possible to obtain a GM PD35 LTE4 up to a maximum concentration of 5 nmol LTE4 ($p < 0.005$). Thus, LTC4- and LTE4-induced bronchoconstrictions are both inhibited by SK&F 104353.

? t s11/7/1-7
11/7/3
DIALOG(R)File 5:Biosis Previews(R)

07437272 BIOSIS NO.: 000091043261
THE EFFECT OF LEUKOTRIENE B-4 INHALATION ON AIRWAY RESPONSIVENESS IN DOGS
AUTHOR: IMAI T; NAMBU F; ADACHI M; TAKAHASHI T; SAITO C; MAEDA M; TSUJI A
AUTHOR ADDRESS: THE FIRST DEP. INTERNAL MED., SCH. MED., SHOWA UNIVERSITY, JAPAN.
JOURNAL: JPN J ALLERGOL 39 (10). 1990. 1380-1387. 1990
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: We studied the effect of **%%%leukotriene%%% B4 (LTB4) %%%inhalation%%% on airway responsiveness in 12 dogs. LTB4 (10 .mu.g/ml) was delivered as an aerosol, generated from a Devilbiss 646 nebulizer** for ten minutes. Airway responsiveness to inhaled methacholine was determined by modified Astograph (7 Hz oscillation method) 1 hr ($n = 6$) and 6 hr ($n = 6$) after LTB4 inhalation. After measurement of airway responsiveness, total cell counts, differential cell counts, thromboxane B2 (TxB2) and 6-keto-prostaglandin (PG)F1.alpha. levels in bronchoalveolar lavage fluid (BALF) were measured. The total cell counts in BALF increased after LTB4 inhalation ($p < 0.05$), and the neutrophil counts in BALF increased significantly 1 hr ($p < 0.05$) and 6 hr after ($p < 0.01$) LTB4 inhalation. Airway responsiveness to inhaled methacholine decreased significantly 1 hr ($p < 0.05$) and 6 hr ($p < 0.01$) after LTB4 inhalation. There were no significant changes in the levels of TxB2 or 6-keto-PGF1.alpha. in BALF 1 hr and 6 hr after LTB4 inhalation. These results suggest that inhaled LTB4 causes neutrophil recruitment into the airway but does not increase airway responsiveness to inhaled methacholine, and the possibility that LTB4 reduces airway responsiveness to inhaled methacholine exists in dogs.

11/7/5
DIALOG(R)File 5:Biosis Previews(R)

06251977 BIOSIS NO.: 000086086160
HYPOXIA-INDUCED ENHANCEMENT OF NONSPECIFIC BRONCHIAL REACTIVITY ROLE OF LEUKOTRIENES
AUTHOR: D'BROT J; AHMED T
AUTHOR ADDRESS: DIV. PULMONARY DISEASE, UNIV. MIAMI SCH. MED., MOUNT SINAI MED. CENT., MIAMI BEACH, FLORIDA 33140.
JOURNAL: J APPL PHYSIOL 65 (1). 1988. 194-199. 1988
FULL JOURNAL NAME: Journal of Applied Physiology
CODEN: JAPHE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Because alveolar hypoxia has been shown to cause an increase of leukotrienes in lung lavage fluid, we tested the hypothesis that enhancement of nonspecific bronchial reactivity during alveolar hypoxia may be mediated by leukotrienes. In nine conscious sheep we determined specific lung resistance (sRL) before and after exposure to either air or a hypoxic gas mixture (13% O2) for 30 min. The sheep then inhaled 50 breaths of aerosolized 5% histamine solution ($n = 6$) or 10 breaths of 2.5% carbachol solution ($n = 6$) on different days, and the measurements of sRL were repeated. On subsequent days the above protocols were repeated after pretreatment with aerosolized. FPL 57231 (3 ml, 1% solution), a %%%leukotriene%%% receptor antagonist. %%%Inhalation%%% of histamine and carbachol after exposure to air caused an increase in means

sRL to 337 and 342% of base line, respectively (P <0.05). Exposure to the hypoxic gas mixture had no effect on sRL but enhanced the histamine- and carbachol-induced increases in mean sRL to 621 and 646% of base line, respectively (P<0.05); these increases were significantly higher than those observed after air exposure (P<0.05). FPL 57231 prevented the hypoxia-induced enhancement of bronchial reactivity to histamine and carbachol without affecting the airway responsivenss to these agents after air. In another group of eight sheep, **aerosolized leukotriene C4**, at a dose (50 .mu.g) that per se had no affect on sRL, enhanced the bronchial reactivity to carbachol. These data suggest that in sheep during alveolar hypoxia airway hyperresponsiveness may be due to the priming of airway smooth muscle by leukotrienes.

11/7/6
DIALOG(R)File 5:Biosis Previews(R)

04740086 BIOSIS NO.: 000080043213
THE EFFECT OF TRH ON THE PERIPHERAL AIRWAY RESPONSE INDUCED BY LEUKOTRIENE D
AUTHOR: KOSHINO T; FUJIMURA M; NISHIOKA S; OKAFUJI K; MINAMI S; KANAMORI K; MATSUDA T; KITAO T; ISHIZAKI T; ET AL
AUTHOR ADDRESS: THIRD DEPARTMENT MEDICINE, SCHOOL MEDICINE, KANAZAWA UNIVERSITY.
JOURNAL: JPN J ALLERGOL 33 (12). 1984 (RECD. 1985). 1059-1062. 1984
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: The effect of TRH on bronchoconstriction in guinea-pigs induced by **%%%leukotriene%%% D4 %%%inhalation%%%** was investigated. Mean pulmonary resistance (RI) and dynamic compliance (Cdyn) were measured using a bodyplethysmograph for small animals and calculated by a microcomputor. Five minutes following the %%%leukotriene%%% D4 %%%inhalation%%%, Cdyn and RL of the control group were -70.7 .+-. 11.3% and +86.9 .+-. 26.3%, those of the TRH (1 mg/kg) pretreated group -60.2 .+-. 11.1% and +78.8 .+-. 27.8% and those of the TRH (2 mg/kg) pretreated group -51.0 .+-. 14.5% (P < 0.05) and +81.6 .+-. 27.7%, respectively. Administration of TRH (2 mg/kg) 6 min after %%%leukotriene%%% D4 %%%inhalation%%% exerted no influence on the effect of leukotriene D4 on Cdyn and RL. Evidently, the sensitivity of the peripheral airway response to leukotriene D4 was decreased by the pretreatment with TRH.

11/7/7
DIALOG(R)File 5:Biosis Previews(R)

04211832 BIOSIS NO.: 000077037877
INHIBITORY EFFECTS OF STEROIDS ON SLOW REACTING SUBSTANCE OF ANAPHYLAXIS MEDIATED BRONCHO CONSTRICTION IN THE GUINEA-PIG IN-VIVO EVALUATION WITH INHALATION OF ANTIGEN AND LEUKOTRIENE C-4
AUTHOR: FUJIMURA M
AUTHOR ADDRESS: THIRD DEP. INTERNAL MED., KANAZAWA UNIV., SCH. MED.
JOURNAL: JPN J ALLERGOL 32 (7). 1983. 365-375. 1983
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Steroids are widely used in the treatment of bronchial asthma. In vitro experiments demonstrate that steroids inhibit synthesis of slow-reacting substance of anaphylaxis (SRS-A) from arachidonic acid. Using a recently developed **nebulizer**, the inhibitory effects of steroids on SRS-A mediated bronchoconstriction induced by inhalation of leukotriene C4 and antigen was studied in vivo in passively sensitized guinea pigs. Mean pulmonary resistance (RL) and dynamic compliance (Cdyn) were measured for objective parameters at airway response. Dexamethasone phosphate (20 mg/kg) was i.p. administered 18-22 h before inhalation of

antigen or leukotriene C4. This pretreatment inhibited the SRS-A mediated bronchoconstriction induced by antigen inhalation, but not that induced by **%%%leukotriene%%% C4 %%%inhalation%%%**. The inhibitory effects of steroids were more remarkable on Cdyn than EL, and also in the later phase than in the earlier phase after antigen inhalation. Steroids apparently inhibit synthesis and/or release of SRS-A, in particular in the peripheral airways, but do not directly block the action of SRS-A.

? t s12/3/100-176
12/3/101
DIALOG(R)File 5:Biosis Previews(R)

07911966 BIOSIS NO.: 000093011089
INTERACTION OF THROMBOXANE A2 AND LEUKOTRIENES IN GUINEA-PIG AIRWAYS IN-VIVO
AUTHOR: FUJIMURA M; BANDO T; MIZUHASHI K; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV., SCH. MED., 13-1 TAKARA-MACHI, 920 KANAZAWA, JPN.
JOURNAL: PROSTAGLANDINS 42 (4). 1991. 379-389. 1991
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/102
DIALOG(R)File 5:Biosis Previews(R)

07910042 BIOSIS NO.: 000093009165
INHIBITORY EFFECT OF INHALATION OF A THROMBOXANE SYNTHETASE INHIBITOR ON BRONCHOCONSTRICTION INDUCED BY **AEROSOLIZED LEUKOTRIENE C-4** AND THROMBOXANE A-2 ANALOGUE IN ANESTHETIZED GUINEA-PIGS
AUTHOR: FUJIMURA M; OGAWA H; SAITO M; SAKAMOTO S; MIYAKE Y; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA 920, JPN.
JOURNAL: ALLERGY (CPH) 46 (7). 1991. 534-539. 1991
CODEN: LLRGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/105
DIALOG(R)File 5:Biosis Previews(R)

07890994 BIOSIS NO.: 000092140297
A NOVEL METHOD FOR THE EVALUATION OF BRONCHOACTIVE AGENTS IN THE CONSCIOUS GUINEA-PIG
AUTHOR: BALL D I; COLEMAN R A; HARTLEY R W; NEWBERRY A
AUTHOR ADDRESS: DEP. PERIPHERAL PHARMACOL., GLAXO GROUP RES. LTD., WARE, HERTS. SG12 0DP, UK.
JOURNAL: J PHARMACOL METHODS 26 (3). 1991. 187-202. 1991
FULL JOURNAL NAME: Journal of Pharmacological Methods
CODEN: JPMED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/107
DIALOG(R)File 5:Biosis Previews(R)

07822846 BIOSIS NO.: 000092104032
THE EFFECT OF INHALATION OF THE LEUKOTRIENE RECEPTOR ANTAGONIST SKF-104353 ON LEUKOTRIENE C-4-INDUCED AND LEUKOTRIENE E-4-INDUCED BRONCHOCONSTRICTION IN SUBJECTS WITH ASTHMA
AUTHOR: CHRISTIE P E; SPUR B W; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY ALLIED RESPIRATORY DISORDERS, 4TH FLOOR, HUNT'S HOUSE, GUY'S HOSPITAL, LONDON SE1 9RT, ENGLAND.
JOURNAL: J ALLERGY CLIN IMMUNOL 88 (2). 1991. 193-198. 1991

FULL JOURNAL NAME: Journal of Allergy and Clinical Immunology
CODEN: JACIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/113
DIALOG(R)File 5:Biosis Previews(R)

07437272 BIOSIS NO.: 000091043261
THE EFFECT OF LEUKOTRIENE B-4 INHALATION ON AIRWAY RESPONSIVENESS IN DOGS
AUTHOR: IMAI T; NAMBU F; ADACHI M; TAKAHASHI T; SAITO C; MAEDA M; TSUJI A
AUTHOR ADDRESS: THE FIRST DEP. INTERNAL MED., SCH. MED., SHOWA UNIVERSITY, JAPAN.
JOURNAL: JPN J ALLERGOL 39 (10). 1990. 1380-1387. 1990
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

12/3/139
DIALOG(R)File 5:Biosis Previews(R)

06636025 BIOSIS NO.: 000087078188
INTERACTIONS OF INHALED **LTC-4** WITH HISTAMINE AND PGD-2 ON AIRWAY CALIBER IN ASTHMA
AUTHOR: PHILLIPS G D; HOLGATE S T
AUTHOR ADDRESS: IMMUNOPHARMACOL. GROUP, SOUTHAMPTON GENERAL HOSP., SOUTHAMPTON SO9 4XY, UNITED KINGDOM.
JOURNAL: J APPL PHYSIOL 66 (1). 1989. 304-312. 1989
FULL JOURNAL NAME: Journal of Applied Physiology
CODEN: JAPHE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/142
DIALOG(R)File 5:Biosis Previews(R)

06588408 BIOSIS NO.: 000087030570
THE EFFECTS OF **INHALED LEUKOTRIENE E-4** ON THE AIRWAY RESPONSIVENESS TO HISTAMINE IN SUBJECTS WITH ASTHMA AND NORMAL SUBJECTS
AUTHOR: ARM J P; SPUR B W; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY ALLIED RESPIRATORY DISORD., 4TH FLOOR, HUNTS HOUSE, GUY'S HOSP., LONDON SE1 9RT, UK.
JOURNAL: J ALLERGY CLIN IMMUNOL 82 (4). 1988. 654-660. 1988
FULL JOURNAL NAME: Journal of Allergy and Clinical Immunology
CODEN: JACIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/149
DIALOG(R)File 5:Biosis Previews(R)

06166028 BIOSIS NO.: 000086000210
SECONDARY RELEASE OF THROMBOXANE A2 IN **AEROSOL LEUKOTRIENE C4**-INDUCED BRONCHOCONSTRICTION IN GUINEA-PIGS
AUTHOR: FUJIMURA M; MIYAKE Y; UOTANI K; KANAMORI K; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA, JPN.
JOURNAL: PROSTAGLANDINS 35 (3). 1988. 427-436. 1988
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/7/2
DIALOG(R)File 5:Biosis Previews(R)

13557524 BIOSIS NO.: 200200186345
The effect of leukotriene D4 inhalation on the antigen-induced airway hyperresponsiveness and inflammation in 5-lipoxygenase gene-deficient mice.
AUTHOR: Kawada Naoki; Yamada Takatoshi; Takahashi Yoshimasa; Tokuoka Shouta ; Masuda Taisei; Tanaka Hiroyuki; Nagai Hiroichi(a)
AUTHOR ADDRESS: (a)Department of Pharmacology, Gifu Pharmaceutical University, 5-6-1 Mitahora-higashi, Gifu, 502-8585**Japan E-Mail: nagai@gifu-pu.ac.jp
JOURNAL: International Archives of Allergy and Immunology 126 (4):p309-317 December, 2001
MEDIUM: print
ISSN: 1018-2438
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background: The role of 5-lipoxygenase (5-LO) products in the asthmatic bronchoconstriction is evident. However, the role of 5-LO products in airway hyperresponsiveness (AHR) and airway inflammation is still under discussion. The aim of the present study is to investigate the role of %%%leukotriene%%% D4 (LTD4) in AHR and allergic airway eosinophilia in mice. Methods: The effect of **LTD4 %%%inhalation%%%** on antigen-induced AHR and airway eosinophilia was investigated in 5-LO gene-deficient mice. Results: After three inhalations of LTD4, airway responsiveness to acetylcholine was not altered in normal or allergic wild-type and 5-LO knockout (KO) mice. In contrast, the number of eosinophils in 5-LO KO allergic mice increased to the level of wild-type allergic mice after the %%%inhalation%%% of LTD4. These observations were confirmed by a histopathological study of the lungs. No change in the cytokine levels in bronchoalveolar lavage fluid and serum immunoglobulin levels was shown after LTD4 %%%inhalation%%%. Conclusion: These findings suggest that LTD4 plays a role in eosinophilic airway inflammation but not in AHR in mice.

12/7/12
DIALOG(R)File 5:Biosis Previews(R)

12816353 BIOSIS NO.: 200100023502
Exhaled nitric oxide following leukotriene E4 and methacholine inhalation in patients with asthma.
AUTHOR: Deykin Aaron; Belostotsky Olga; Hong Christopher; Massaro Anthony F ; Lilly Craig M; Israel Elliot(a)
AUTHOR ADDRESS: (a)Pulmonary Division, Brigham and Women's Hospital, 75 Francis Street, Boston, MA, 02115: eisrael@rics.bwh.harvard.edu**USA
JOURNAL: American Journal of Respiratory and Critical Care Medicine 162 (5):p1685-1689 November, 2000
MEDIUM: print
ISSN: 1073-449X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Nitric oxide (NO) is a molecular gas that can be recovered in higher levels from the exhaled gas of subjects with asthma than from subjects without asthma. However, the precise mechanisms responsible of promoting increased fraction of expired nitric oxide (FENO) in asthma are unknown. As %%%leukotriene%%% antagonism has been shown to reduce FENO in patients with asthma, we hypothesized that leukotrienes mediate the increased FENO encountered in this condition. Furthermore, because %%%leukotriene%%% antagonism stabilizes serum eosinophil markers during reductions in inhaled corticosteroid doses, and FENO has been shown to correlate with sputum eosinophils in asthma, we reasoned that the effect of leukotrienes on FENO might be mediated by eosinophils recruited to the

airway by leukotrienes. To test this hypothesis, we performed methacholine and %%%leukotriene%%% (LT) E4 bronchoprovocation challenges in 16 subjects with atopic asthma and measured FENO and sputum differential counts before and after bronchoprovocation. We then compared FENO in the seven subjects who developed increased sputum eosinophils following **LTE4 %%%inhalation%%%** with values measured after methacholine %%%inhalation%%% in these seven subjects. Following LTE4 %%%inhalation%%% , eosinophils rose from 4.01 +- 0.89% pre-LTE4 to 8.33 +- 1.52% post-LTE4. The mean change in sputum eosinophils from baseline after LTE4 %%%inhalation%%% was larger than that after methacholine %%%inhalation%%% (+4.31 +- 1.25% versus -1.14 +- 0.93%). After LTE4 %%%inhalation%%%, FENO levels did not differ from pre-challenge baseline or from levels following methacholine %%%inhalation%%% (ANOVA p > 0.05). These data indicate that neither LTE4 nor recruitment of eosinophils into the airway by LTE4 is a sufficient stimulus to acutely increase FENO in subjects with asthma.

12/7/28
DIALOG(R)File 5:Biosis Previews(R)

12039651 BIOSIS NO.: 199900320170
Effect of inhaled leukotriene D4 on airway eosinophilia and airway hyperresponsiveness in asthmatic subjects.
AUTHOR: Mulder Alma; Gauvreau Gail M; Watson Rick M; O'Byrne Paul M(a)
AUTHOR ADDRESS: (a)Department of Medicine, Health Sciences Center, McMaster University, 1200 Main St. West, Rm. 3U-**Canada
JOURNAL: American Journal of Respiratory and Critical Care Medicine 159 (5 PART 1):p1562-1567 May, 1999
ISSN: 1073-449X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Inhaled cysteinyl leukotrienes may cause recruitment of eosinophils into asthmatic airways. We compared the effects of **inhaled %%%leukotriene%%% D4 (LTD4)**, methacholine, and allergen on airway eosinophils in 10 nonsmoking, atopic, mildly asthmatic subjects in a double-blind, diluent-controlled, randomized crossover study. Concentrations of LTD4, methacholine, and allergen resulting in a 30% decrease in FEV1, and diluent controls (ethanol and saline), were inhaled with at least 7 d between challenges. Spirometry was conducted for 4 h after %%%inhalation%%% challenge, and airway hyperresponsiveness (AHR) to methacholine was measured before and 24 h after challenge. Sputum was induced before and 4 h, 7 h, and 24 h after challenge. The maximum decrease in FEV1 was 31.4 +- 1.8% with LTD4, 39.4 +- 2.8% with methacholine, and 30.1 +- 3.4% with allergen. AHR to methacholine, at the provocative concentration causing a 20% decrease in FEV1 (PC20), was enhanced 24 h after allergen challenge, but remained unchanged 24 h after LTD4 and methacholine (p > 0.05). The percentage of eosinophils in sputum was increased after %%%inhalation%%% of allergen at 7 h and 24 h (p = 0.003), but not after LTD4 or methacholine (p = 0.70). We demonstrated that neither %%%inhalation%%% of LTD4 nor of methacholine at concentrations causing submaximal bronchoconstriction increases the number of sputum eosinophils in the airways of mildly asthmatic subjects. However, LTD4 may still be an important cofactor for eosinophil recruitment in asthma.

12/7/29
12/7/43
DIALOG(R)File 5:Biosis Previews(R)

10981043 BIOSIS NO.: 199799602188
The effect of **inhaled leukotriene B-4** in normal and in asthmatic subjects.
AUTHOR: Sampson Sally E; Costello John F; Sampson Anthony P(a)
AUTHOR ADDRESS: (a)Immunopharmacol. Group, Level F, Centre Block, Southampton Gen. Hosp., Southampton, SO16 6YD**UK
JOURNAL: American Journal of Respiratory and Critical Care Medicine 155 (5):p1789-1792 1997

12/3/150
DIALOG(R)File 5:Biosis Previews(R)

06110721 BIOSIS NO.: 000085073871
BRONCHIAL RESPONSIVENESS TO **INHALED LEUKOTRIENE D-4** IN BRONCHIAL ASTHMA
PART 2. INFLUENCE OF VAGAL REFLEX ON THE BRONCHOCONSTRICTION CAUSED BY INHALED LEUKOTRIENE D-4
AUTHOR: YAMAI T; YUKAWA T; FUKUDA T; MAKINO S
AUTHOR ADDRESS: DEP. MED. CLINICAL IMMUNOLOGY, DOKKYO UNIV. SCH. MED.
JOURNAL: JPN J ALLERGOL 36 (10). 1987. 893-901. 1987
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

12/3/151
DIALOG(R)File 5:Biosis Previews(R)

06080575 BIOSIS NO.: 000085043724
BRONCHIAL RESPONSIVENESS TO INHALED LEUKOTRIENE D-4 IN BRONCHIAL ASTHMA
AUTHOR: YAMAI T; FUKUDA T; MAKINO S
AUTHOR ADDRESS: DEP. MED. CLINICAL IMMUNOL., DOKKYO UNIV. SCH. MED.
JOURNAL: JPN J ALLERGOL 36 (9). 1987. 838-847. 1987
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

12/3/154
DIALOG(R)File 5:Biosis Previews(R)

06056812 BIOSIS NO.: 000085019961
EFFECTS OF **LEUKOTRIENE B-4 INHALATION AIRWAY** SENSITIZATION AND LUNG GRANULOCYTE INFILTRATION IN THE GUINEA-PIG
AUTHOR: SILBAUGH S A; STENGEL P W; WILLIAMS G D; HERRON D K; GALLAGHER P; BAKER S R
AUTHOR ADDRESS: DEP. CONNECTIVE TISSUE PULM. RES., MC620, LILLY RES. LAB., LILLY CORP. CENT., INDIANAPOLIS, INDIANA, 46285.
JOURNAL: AM REV RESPIR DIS 136 (4). 1987. 930-934. 1987
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/156
DIALOG(R)File 5:Biosis Previews(R)

05735120 BIOSIS NO.: 000084083526
NEBULIZATION AND SELECTIVE DEPOSITION OF LTD-4 IN HUMAN LUNGS
AUTHOR: BISGAARD H; POULSEN L; SONDERGAARD I
AUTHOR ADDRESS: VESTER SOGADE 187, DK-1601 COPENHAGEN, DEN.
JOURNAL: ALLERGY (COPENH) 42 (5). 1987. 336-342. 1987
FULL JOURNAL NAME: ALLERGY (Copenhagen)
CODEN: LLRGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/159
DIALOG(R)File 5:Biosis Previews(R)

05662894 BIOSIS NO.: 000084011299
BRONCHIAL EFFECTS OF **LEUKOTRIENE D-4 INHALATION** IN NORMAL HUMAN LUNG
AUTHOR: BISGAARD H; GROTH S
AUTHOR ADDRESS: VESTER SOGADE 18, 7.TH., DK-1601 COPENHAGEN, DENMARK.

JOURNAL: CLIN SCI (LOND) 72 (5). 1987. 585-592. 1987
FULL JOURNAL NAME: Clinical Science (London)
CODEN: CSCIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/171
DIALOG(R)File 5:Biosis Previews(R)

04713033 BIOSIS NO.: 000080016159
THE EFFECT OF **INHALED LEUKOTRIENE D-4** IN HUMANS
AUTHOR: SMITH L J; GREENBERGER P A; PATTERSON R; KRELL R D; BERNSTEIN P R
AUTHOR ADDRESS: PULMONARY SECT., NORTHWESTERN UNIV. MED. CENT., 250 E. SUPERIOR ST., WESLEY 456, CHICAGO, ILL. 60611.
JOURNAL: AM REV RESPIR DIS 131 (3). 1985. 368-372. 1985
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

12/3/176
DIALOG(R)File 5:Biosis Previews(R)

03974343 BIOSIS NO.: 000076059909
AIRWAY CONSTRICTION IN NORMAL HUMANS PRODUCED BY **INHALATION OF LEUKOTRIENE D** POTENCY TIME COURSE AND EFFECT OF ASPIRIN THERAPY
AUTHOR: WEISS J W; DRAZEN J M; MCFADDEN E R JR; WELLER P; COREY E J; LEWIS R A; AUSTEN K F
AUTHOR ADDRESS: SEELEY G. MUDD BUILD., 6TH FLOOR, 250 LONGWOOD AVE., BOSTON, MASS. 02115.
JOURNAL: JAMA (J AM MED ASSOC) 249 (20). 1983. 2814-2817. 1983
FULL JOURNAL NAME: JAMA (Journal of the American Medical Association)
CODEN: JAMAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

? t s12/7/149, 152, 153

12/7/149
DIALOG(R)File 5:Biosis Previews(R)

06166028 BIOSIS NO.: 000086000210
SECONDARY RELEASE OF THROMBOXANE A2 IN AEROSOL LEUKOTRIENE C4-INDUCED BRONCHOCONSTRICTION IN GUINEA-PIGS
AUTHOR: FUJIMURA M; MIYAKE Y; UOTANI K; KANAMORI K; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA, JPN.
JOURNAL: PROSTAGLANDINS 35 (3). 1988. 427-436. 1988
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effect of a thromboxane synthetase inhibitor (OKY-046) on bronchconstriction induced by **aerosol %%%leukotriene%%% C4** and histamine was studied in anesthetized, artificially ventilated guinea pigs in order to examine whether secondary release of thromboxane A2 is produced by aerosol %%%leukotriene%%% C4 or not. 0.01-1.0.mu.g/ml of %%%leukotriene%%% C4 and 12.5-400 .mu.g/ml of histamine inhaled from ultrasonic nebulizer developed for small animals caused dose-dependent increase of pressure at airway opening (Pao) which is considered to be an index representing bronchial response. Pretreatment of the animals with intravenous OKY-046 (100mg/kg) significantly reduced the airway responses produced by %%%inhalation%%% of 0.1, 0.33 and 1.0.mu.g/ml of %%%leukotriene%%% C4, while the pretreatment did not affect the histamine dose-response curve. Based on these findings and previous reports (6,7), it is suggested that aerosol %%%leukotriene%%% C4 activates arachidonate cyclooxygenase pathway including thromboxane A2 synthesis and the

released cyclooxygenase products have a bronchodilating effect as a whole.

12/7/153
DIALOG(R)File 5:Biosis Previews(R)

06077898 BIOSIS NO.: 000085041047
PULMONARY GAS TRAPPING IN THE GUINEA-PIG AND ITS APPLICATION IN PHARMACOLOGICAL TESTING
AUTHOR: SILBAUGH S A; STENGEL P W; DILLARD R D; BEMIS K G
AUTHOR ADDRESS: DEP. CONNECTIVE TISSUE PULMONARY RES., MC620, LILLY RES. LAB., LILLY CORP. CENT., INDIANAPOLIS, INDIANA 46285.
JOURNAL: J PHARMACOL METHODS 18 (4). 1987. 295-304. 1987
FULL JOURNAL NAME: Journal of Pharmacological Methods
CODEN: JPMED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Airway constriction produced by bronchoconstrictive aerosols in vivo can result in substantial postmortem pulmonary gas trapping in the guinea pig. In order to use gas trapping responses for the evaluation of potential antiasthma agents, we developed a multiple animal %%%inhalation%%% exposure apparatus and an accurate system for quantitating excised lung gas volumes in the guinea pig. **Aerosols of histamine, methacholine, and %%%leukotriene%%% D4** were shown to produce gas trapping responses that were inhibited in a dose-dependent fashion by appropriate antagonists. The approach described provides an objective and sensitive measure of the severity of airway obstruction, does not require surgery or anesthesia, and allows excellent control of unwanted sources of experimental variation.

? t s7/7/157

7/7/157
DIALOG(R)File 5:Biosis Previews(R)

07910042 BIOSIS NO.: 000093009165
INHIBITORY EFFECT OF %%%INHALATION%%% OF A THROMBOXANE SYNTHETASE INHIBITOR ON BRONCHOCONSTRICTION INDUCED BY AEROSOLIZED %%%LEUKOTRIENE%%% C-4 AND THROMBOXANE A-2 ANALOGUE IN ANESTHETIZED GUINEA-PIGS
AUTHOR: FUJIMURA M; OGAWA H; SAITO M; SAKAMOTO S; MIYAKE Y; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA 920, JPN.
JOURNAL: ALLERGY (CPH) 46 (7). 1991. 534-539. 1991
CODEN: LLRGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effect of aerosol administration of a thromboxane synthetase inhibitor (OKY-046) on bronchoconstriction induced by **aerosol %%%leukotriene%%% C4,** histamine and a thromboxane A2 analogue (STA2) was studied in anesthetized, artificially ventilated guinea pigs in order to evaluate the effectiveness of %%%inhalation%%% of OKY-046 on an unfavorable mechanism of secondary release of thromboxane A2. 0.01-1.0 .mu.g/ml %%%leukotriene%%% C4, 25-400 .mu.g/ml histamine and 0.033-1.0 .mu.g/ml STA2 inhaled from an ultrasonic nebulizer developed for small animals caused a dose-dependent increase of pressure at the airway opening (Pao), which is considered to be an index representing bronchial response. Pretreatment of the animals with aerosol OKY-046 (0.035 and 0.35 mg/animal) significantly reduced the airway responses produced by %%%inhalation%%% of %%%leukotriene%%% C4 and STA2, in a dose-dependent manner, while the pretreatment did not affect the histamine dose-response curve. These findings suggest that aerosol %%%leukotriene%%% C4 and STA2 activate thromboxane synthesis in the airway, and %%%inhalation%%% of OKY-046 may be useful for preventing the secondary release of thromboxane A2, which is an unfavorable mechanism in asthma.

? t s12/7/1-99

ISSN: 1073-449X
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Leukotriene%%% (LT) B-4 is a potent leukocyte chemotaxin that increases bronchial responsiveness in animal models. In a double-blind, placebo-controlled crossover study we examined the effects of LTB-4 on lung function, bronchial responsiveness, and blood leukocyte counts in six normal subjects and in six subjects with mild asthma who inhaled mean +- SEM doses of 17.6 +- 3.4 and 18.2 +- 1.9 mu-g LTB-4, respectively, or placebo. There were no significant changes in specific airway conductance or bronchial responsiveness in either normal subjects or asthmatics for as long as 24 h after %%%inhalation%%%. In the normal subjects, LTB-4 rapidly reduced blood neutrophil counts to 19.8 +- 6.3% of baseline at 5 min (p = 0.0003 compared with placebo), followed by a neutrophilia of 307 +- 40% of baseline at 30 min (p = 0.007). Similar changes occurred in asthmatics, with a neutropenia at 5 min (69.6 +- 5.8%; p = 0.003) and a neutrophilia at 30 min (183 +- 17.2%; p = 0.037). The neutrophilia was not sustained in either subject group, with values being no different from that of placebo by 6 h. The asthmatics had significantly less neutropenia (p = 0.005) and less neutrophilia (p = 0.018) than did the normal subjects. Placebo %%%inhalation%%% had no effect on any parameter in either group. The smaller neutrophil responses in asthmatics may reflect desensitization of blood neutrophils in vivo because of chronic exposure to endogenous LTB-4.

12/7/46
DIALOG(R)File 5:Biosis Previews(R)

10904171 BIOSIS NO.: 199799525316
The effect of inhaled leukotriene D-4 and methacholine on sputum cell differentials in asthma.
AUTHOR: Diamant Zuzana; Hiltermann Jeroen T; Van Rensen Elizabeth L; Callenbach Petra M; Veselic-Charvat Maud; Van Der Veen Hilly; Sont Jacob K; Sterk Peter J
AUTHOR ADDRESS: Lung Function Lab., C2-P, Leiden Univ. Med. Cent., P.O. Box 9600, NL-2300 RC Leiden**Netherlands
JOURNAL: American Journal of Respiratory and Critical Care Medicine 155 (4):p1247-1253 1997
ISSN: 1073-449X
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The cysteinyl %%%leukotriene%%% LTE-4 has been shown to induce airway eosinophilia in asthmatics in vivo. This phenomenon has not yet been reported for LTD-4. Hence, we examined the effect of **inhaled LTD-4** and a control bronchoconstrictor agent, methacholine, on cell differentials in hypertonic saline-induced whole sputum samples of 12 nonsmoking atopic asthmatic subjects (three women, nine men; 21 to 29 yr of age; FEV-1, 74 to 120% pred; PC-20FEV-1 methacholine lt 9.6 mg/ml). The study had a crossover, placebo-controlled design consisting of 4 d separated by gtoreq 1 wk. On each randomized study day, the subjects inhaled five serial doses of either LTD-4 (mean cumulative concentration: 95.7 mu-M) or methacholine (mean cumulative concentration: 542 mM) or five doses of their respective diluents (PBS/ethanol or PBS). The airway response was measured by FEV-1, followed by sputum induction with 4.5% NaCl, 4 h postchallenge. Inflammatory cells (gtoreq 250) were counted twice on coded cytospins and expressed as percentages of nonsquamous cells. There was no significant difference in the maximal percent fall in FEV-1 from baseline between LTD-4 (mean +- SEM, 49.5 +- 4.4% fall) and methacholine (mean +- SEM, 55.9 +- 3.4% fall) (p = 0.11). LTD-4 induced a significant increase in the percentage of sputum eosinophils as compared with its diluent (mean +- SD, 26.6 +- 21.3% and 10.2 +- 8.8%, respectively, p = 0.025), whereas a similar trend for methacholine failed to reach significance (mean +- SD, 19.1 +- 22.9% and 7.8 +- 5.8%, respectively; p = 0.11). There was no significant difference in the changes in the percentage of sputum eosinophils between LTD-4 and methacholine (mean difference +- SD, 7.5 +- 12.5% eosinophils; p = 0.09). We conclude that LTD-4 induces eosinophilia in sputum of asthmatic subjects 4 h after %%%inhalation%%%. Our data suggest that LTD-4 recruits

eosinophils into the airways of asthmatics in vivo, possibly by virtue of direct or indirect chemotactic properties, whereas an additional effect of vigourous airway narrowing per se cannot be excluded.

12/7/51

12/7/54
DIALOG(R)File 5:Biosis Previews(R)

10377438 BIOSIS NO.: 199698832356
Involvement of endogenous tachykinins in LTD-4-induced airway responses.
AUTHOR: Ishikawa J; Ichinose M; Miura M; Kageyama N; Yamauchi H; Tomaki M; Sasaki Y; Shirato K(a)
AUTHOR ADDRESS: (a)First Dep. Internal Med., Tohoku Univ. Sch. Med., 1-1 Seiryo-machi, Aoba-ku, Sendai 980**Japan
JOURNAL: European Respiratory Journal 9 (3):p486-492 1996
ISSN: 0903-1936
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Leukotriene%%% D-4-(LTD-4) has been reported to cause tachykinin release from airway sensory nerves. However, the functional significance of endogenously released tachykinins in LTD-4-mediated airway responses has not been fully clarified. The aim of this study was to investigate whether LTD-4-induced airway responses are due, in part, to tachykinin release in guinea-pigs. Airway plasma exudation and bronchoconstriction were assessed by measuring extravasation of Evans blue dye and by mean pulmonary resistance (RL) in the presence of atropine (1 mg.kg-, i.v.) and propranolol (1 mg cntdot kg-1 i.v.), respectively. LTD-4 (5 mu-g cntdot mL-1 for 1 min) %%%inhalation%%% caused increase in plasma exudation and RL. Capsaicin pretreatment of animals to deplete sensory neuropeptides significantly inhibited LTD-4-induced plasma exudation in the main bronchi, but not in the central (cIPA) and peripheral intrapulmonary airways (pIPA). Pretreatment with specific tachykinin neurokinin-1 (NK-1)-receptor antagonists, FK 888 (10 mg cntdot kg-1 i.v.) and CP 96345 (4 mg cntdot kg-1 i.v.), also significantly reduced LTD4-induced plasma exudation in the main bronchi, and in the main bronchi and cIPA, respectively. However, these antagonists did not significantly affect the LTD-4-induced increase in RL. In contrast, neurokinin-2 (NK-2)-receptor antagonist, SR 48968 (0.3 mg cntdot kg-1 iv.), significantly inhibited the bronchoconstriction **after LTD-4-%%%inhalation%%%**. These results suggest that %%%leukotriene%%% D-4-induced bronchoconstriction and plasma exudation in guinea-pigs are, in part, due to tachykinin release from airway sensory nerves.

12/7/56
DIALOG(R)File 5:Biosis Previews(R)

10344616 BIOSIS NO.: 199698799534
Aerosolized LTB-4 produces delayed onset increases in pulmonary gas trapping.
AUTHOR: Silbaugh S A(a); Stengel P W; Cockerham S L; Froelich L L; Bendele A M; Rippy M K; Baker S R; Sofia M J; Jackson W T
AUTHOR ADDRESS: (a)Lilly Res. Lab., Eli Lilly Co., Lilly Corp. Cent., Indianapolis, IN 46285**USA
JOURNAL: Prostaglandins Leukotrienes and Essential Fatty Acids 54 (2):p 115-121 1996
ISSN: 0952-3278
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Airway obstruction, as measured by increases in postmortem pulmonary gas trapping, and lung inflammatory changes were examined in guinea pigs exposed for up to 4 h to **aerosols of %%%leukotriene%%% B-4**

(LTB-4) or its non-chemotactic isomer, 6-trans-12-epi-LTB-4. Airway obstruction and cytological responses in isomer-exposed animals were similar to those of unexposed control animals. LTB-4-exposed animals had minimal inflammatory changes at 0.5 h but became dyspneic by 2 h and had increased airway obstruction, bronchoalveolar lavage neutrophils and eosinophils, and pulmonary tissue granulocyte scores. The LTB-4-induced effects at 4 h were similar to those at 2 h, except for further increases in BAL neutrophils and eosinophils. LTB-4-induced airway obstructive and inflammatory changes were prevented by pretreatment with the LTB-4 receptor antagonist SC-41930, but were unaffected by indomethacin. Thus, prolonged LTB-4 %%%inhalation%%% can produce delayed onset airway obstruction that is stereospecific, cyclooxygenase-independent, and temporally associated with the influx of granulocytes into lung airways.

12/7/72
DIALOG(R)File 5:Biosis Previews(R)

09415361 BIOSIS NO.: 199497423731
Inhibitory effect of aerosol administration of a sulfidopeptide leukotriene antagonist on bronchoconstriction induced by antigen inhalation in guinea pigs.
AUTHOR: Bando T(a); Fujimura M; Shintani H; Saito M; Kurashima K; Nishi K; Matsuda T
AUTHOR ADDRESS: (a)Third Dep. Intern. Med., Kanazawa Univ. Sch. Med., 13-1 Takara-machi, Kanazawa 920**Japan
JOURNAL: Arzneimittel-Forschung 44 (6):p754-757 1994
ISSN: 0004-4172
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English; German

ABSTRACT: The effects of %%%inhalation%%% of the sulfidopeptide %%%leukotriene%%% antagonist AS-35(9-((4-Acetyl-3-hydroxy-2-n-propyl-phenoxy)methyl)-3-(1H-tetrazol-5-yl)-4H-pyrido (1,2-a) pyrimidin-4-one, CAS 108427-72-1) on bronchoconstriction induced by **aerosol antigen, histamine, and %%%leukotriene%%% C4, D4 (LTC4, D4)** were investigated in anesthetized and artificially ventilated guinea pigs. The increase in pressure at the airway opening (P-ao) was measured as an index representing the grade of bronchial response. The bronchoconstriction induced by aerosol antigen was suppressed dose-dependently by pretreatment with inhaled AS-35 (0.1 mg and 1 mg) through a pressurized meter-dosed inhaler in the passively sensitized animals pretreated with diphenhydramine hydrochloride. But the histamine-induced bronchoconstriction was not altered by the pretreatment with AS-35 %%%inhalation%%%. On the other hand, LTC4- and LTD4-induced bronchoconstriction was inhibited by the pretreatment with aerosol AS-35 in a dose-dependent manner. The deposited dose of inhaled AS-35 in the peripheral airways was 3.5 mu-g and 6.5 mu-g when 0.1 mg and 1 mg of the drug was inhaled, respectively. These results suggest that sulfidopeptide leukotrienes (sLTs) play an important role in the allergic bronchoconstriction in guinea pigs pretreated with antihistamine, and AS-35 %%%inhalation%%% may be beneficial in the treatment of asthma.

12/7/75
DIALOG(R)File 5:Biosis Previews(R)

09324624 BIOSIS NO.: 199497332994
Increased urinary LTE-4 excretion following inhalation of LTC-4 and LTE-4 in asthmatic subjects.
AUTHOR: Christie P E; Tagari P; Ford-Hutchinson A W; Black C; Markendorf A; Schmitz-Schumann M; Lee T H(a)
AUTHOR ADDRESS: (a)Dep. Allergy Allied Respiratory Disorders, 4th Flr., Hunts House, Guys Hosp., London SE1 9RT**UK
JOURNAL: European Respiratory Journal 7 (5):p907-913 1994
ISSN: 0903-1936
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Urinary %%%leukotriene%%% E-4 (LTE-4) increases during exacerbations of asthma and following antigen challenge. We determined whether urinary LTE-4 excretion reflects sulphidopeptide leukotrienes in the airways of asthmatic patients. Urinary LTE-4 concentration was measured prior to and 1.5 and 3.5 h following **%%%inhalation%%% of bronchoconstrictive doses of %%%leukotriene%%% C-4 (LTC-4) or LTE-4 in** eight asthmatic subjects. Increasing doses of agonist were inhaled until a 35% fall in specific airways conductance (sGaw) was achieved. There was no significant difference between the 53+-3% (mean+-SEM) fall in sGaw following %%%inhalation%%% of LTC-4 (63.1 ng geometric mean, GM, range 5.8-527.5 ng) and the 43+-4% fall in sGaw following %%%inhalation%%% of LTE-4 7.94 ng/GM (range 1323701 ng). The LTE-4 excretion rate increased significantly from 2.95 (range 0.617.5) ng cntdot h-1 to 4.67 (range 0.8-20) ng cntdot h-1 at 1.5 h following LTC-4 %%%inhalation%%%; and from 1.8 (range 0.07-6.7) ng cntdot h-1 to 6.9 (range 2.9-27.3) ng cntdot h-1 at 1.5 h following LTE-4 %%%inhalation%%%; and had returned from baseline by 3.5 h. There was a correlation between the dose of LTC-4 inhaled and LTE-4 excreted in the urine (r= 0.82 and r=0.72, respectively). The % recovery of LTE-4 in the urine, of the total dose of inhaled LTC-4 or LTE-4 administered, was 6.9+-4.1% and 0.8+-0.3%, respectively. Thus, %%%inhalation%%% of bronchoconstricting doses of LTC-4 or LTE-4 alter urinary LTE-4 excretion in a dose-dependent fashion. This indicates that urinary LTE-4 can be used as a marker of sulphidopeptide %%%leukotriene%%% synthesis in the lungs of patients with asthma.

12/7/86
DIALOG(R)File 5:Biosis Previews(R)

08881060 BIOSIS NO.: 199396032561
Effects of NZ-107 on airway inflammation and cell activation in guinea-pigs.
AUTHOR: Iwama Takehisa(a); Nagai Hiroichi; Koda Akihide
AUTHOR ADDRESS: (a)Dep. Pharmacol., Gifu Pharmaceutical Univ., 5-6-1 Mitahara-higashi, Gifu 502**Japan
JOURNAL: Journal of Pharmacy and Pharmacology 45 (4):p286-291 1993
ISSN: 0022-3573
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The effects of NZ-107 on some airway inflammation models and the generation of superoxide anion (O-2-) were studied in guinea-pigs. Airway inflammation was caused by intra-tracheal injection of murine recombinant interleukin-5 (mrIL-5, 15 mu-g/animal), %%%inhalation%%% of platelet-activating factor (PAF, 0.003%) and **intra-tracheal injection of %%%leukotriene%%% B-4** (LTB-4, 10 mu-g/animal). NZ-107 (4-bromo-5-(3-ethoxy-4-methoxybenzylamino)-3(2H)-pyridazinone) at a dose of 50 mg kg-1, intraperitoneally reduced mrIL-5- and PAF-induced eosinophilia. This compound at a dose of 25 and 50 mg kg-1 also suppressed LTB-4-induced eosinophilia and neutrophilia in bronchoalveolar lavage fluid (BALF). On the other hand, prednisolone at a dose of 20 mg kg-1, i.p., prevented the increased number of macrophages, eosinophils and neutrophils induced by mrIL-5, the increased number of eosinophils induced by PAF and the increased number of eosinophils and neutrophils induced by LTB-4 in BALF. Furthermore, both drugs reduced mrIL-5- or PAF-induced increase in the number of airway epithelial cells in BALF. The generation of O-2- was measured by the method of cytochrome C reduction. NZ-107 (10-100 mu-g mL-1) attenuated PAF- and FMLP-induced O-2- production from macrophages and reduced PAF-induced O-2- generation by eosinophils but had no effect on that from neutrophils. These results indicate that NZ-107 prevents the increased number of pulmonary eosinophils and airway epithelial cells and the activation of macrophages and eosinophils, suggesting that NZ-107 may be useful as a remedy for airway inflammatory diseases such as bronchial asthma.

12/7/96
DIALOG(R)File 5:Biosis Previews(R)

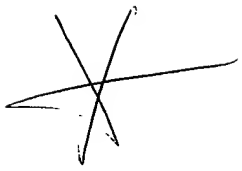
08296561 BIOSIS NO.: 000094067859
THE EFFECTS OF LIPOXIN A-4 ON AIRWAY RESPONSES IN ASTHMATIC SUBJECTS
AUTHOR: CHRISTIE P E; SPUR B W; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY AND ALLIED RESPIRATORY DISORDERS, 4TH FLOOR, HUNTS' HOUSE, GUY'S HOSP., LONDON SW1 9RT, UK.
JOURNAL: AM REV RESPIR DIS 145 (6). 1992. 1281-1284. 1992
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This study was performed to determine whether lipoxin A4 (LXA4) %%%inhalation%%% in asthmatic subjects has an effect on airways response. Eight subjects (six asthmatic, two normal) attended for bronchial %%%inhalation%%% challenge with LXA4. In three of these subjects (two asthmatics, one normal) blood pressure, pulse, and symptoms before and after challenge were recorded. Subsequently five male patients with mild asthma (22 to 34 yr of age) reattended for bronchial **%%%inhalation%%% challenge with either %%%leukotriene%%% C4** (LTC4) or the combination of LTC4 and 1 .times. 10-4 M LXA4. After %%%inhalation%%% of each dose of agonist SGaw and V25 were measured. Airway responsiveness was determined by the concentration of agonist in the nebulizer required to induce a 35% fall in SGaw (PC35). There was no effect of LXA4 %%%inhalation%%% of SGaw, V25, blood pressure, pulse, or symptoms. There was a significant shift of the SGaw and V25 dose-response curve to the right after %%%inhalation%%% challenge with LTC4 combined with 1 .times. 10-4 M LXA4 as compared with that after %%%inhalation%%% challenge with LTC4 alone ($p < 0.01$ and $p < 0.025$, respectively). Thus, LXA4 may modulate LTC4-induced airway obstruction and may act as an endogenous sulfidopeptide %%%leukotriene%%% receptor antagonist.

? t s14/7/1-32

14/7/8
DIALOG(R)File 5:Biosis Previews(R)

10158802 BIOSIS NO.: 199698613720
The promotion of patent airways and inhibition of antigen-induced bronchial obstruction by endogenous nitric oxide.
AUTHOR: Persson Magnus G; Friberg Sten G; Gustafsson Lars E; Hedqvist Per
AUTHOR ADDRESS: Dep. Physiol. Pharmacol., Inst. Environmental Med., Karolinska Inst., S-171 77 Stockholm**Sweden
JOURNAL: British Journal of Pharmacology 116 (7):p2957-2962 1995
ISSN: 0007-1188
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English



ABSTRACT: 1 The aim of the present study was to investigate the role of nitric oxide (NO), histamine and leukotrienes in bronchial obstruction. For this, guinea-pigs immunized against ovalbumin were studied under anaesthesia during challenge with antigen or agonists. 2 Challenge with %%%nebulized%%% antigen (0.1 -1 mg) elicited dose-dependent increases in insulation pressure which were abolished by combined administration of histamine and %%%leukotriene%%% antagonists. 3 Challenge with %%%nebulized%%% antigen (0.1- 1 mg) also elicited dose-dependent increases in the concentration of endogenous nitric oxide in the exhaled air. After an initial peak, exhaled NO concentrations returned to pre-challenge levels. 4 The increase in insufflation pressure and in exhaled NO caused by ovalbumin challenge was inhibited by combined administration of histamine and %%%leukotriene%%% antagonists. 5 In non-immunized guinea-pigs, challenge of the airways with %%%nebulized%%% histamine (10 -1000 nmol) or %%%leukotriene%%% C-4 (LTC-4, 30-300 pmol) elicited dose-dependent increases in insufflation pressure and in concentrations of endogenous NO in exhaled air. 6 The increase in exhaled NO correlated with the increase in insufflation pressure in response to ovalbumin, histamine and LTC-4. An inhibitor of endogenous NO synthesis, N-omega-nitro-L-arginine methylester (L-NAME, 30 mg kg-1 i.v.) abolished NO exhalation, and markedly augmented the airway responses to ovalbumin,

histamine, or LTC-4. 7 The potentiation by L-NAME of the increase in insufflation pressure in response to ovalbumin or histamine was prevented by exogenous NO (20 p.p.m.) in the inhaled air. 8 The results indicate that endogenous NO has an inhibitory effect on bronchial obstruction. Increased NO release during allergen challenge is likely to be due to actions of histamine and leukotrienes.

14/7/9
DIALOG(R)File 5:Biosis Previews(R)

10021353 BIOSIS NO.: 199598476271
Allergen-induced late-phase airways obstruction in the pig: Mediator release and eosinophil recruitment.
AUTHOR: Fornhem C(a); Kumlin M; Lundberg J M; Alving K
AUTHOR ADDRESS: (a)Div. Pharmacology, Dep. Physiology Pharmacology, Karolinska Inst., S-171 77 Stockholm**Sweden
JOURNAL: European Respiratory Journal 8 (7):p1100-1109 1995
ISSN: 0903-1936
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The aim of this study was to develop a novel model for studies of mediator mechanisms involved in the late asthmatic reaction in the lower airways, by using the sensitized pig. The release of histamine and cysteinyl-containing leukotrienes (cys-LTs), as well as the levels of inflammatory cells in blood and bronchoalveolar lavage fluid, were determined and their relationship to plasma cortisol levels and pulmonary airways obstruction was noted. Specific-pathogen free pigs were actively sensitized with Ascaris suum allergen, and one group of animals was treated with a cortisol-synthesis inhibitor (metyrapone) by constant intravenous infusion. Ascaris suum allergen was %%%nebulized%%% into the lower airways and total lung resistance, blood leucocyte count and urinary levels of methylhistamine and %%%leukotriene%%% E-4 (LTE-4) were followed for 8 h, whereafter bronchoalveolar lavage was performed for analysis of leucocytes. An increase in urinary methylhistamine and LTE-4 was seen during the acute allergic reaction in both groups of pigs. Metyrapone treatment prolonged the acute release of histamine, and this was seen together with a prolonged acute bronchoconstrictor response. In metyrapone-treated pigs, a continuous release over 8 h was seen for cys-LTs, but not for histamine. A late blood eosinophilia was also seen in metyrapone-treated animals, starting 4-6 h after allergen challenge. Late cys-LT release and eosmophilia were absent in non-metyrapone-treated animals. These results suggest that allergen-induced late release of cys-LTs as well as blood eosinophilia occur simultaneously with late-phase airways obstruction in the pig, and that all these reactions are prevented by high levels of endogenous cortisol.

14/7/10
DIALOG(R)File 5:Biosis Previews(R)

09660786 BIOSIS NO.: 199598115704
Cyproheptadine-induced attenuation of type-I immediate-hypersensitivity reactions of airway smooth muscle from immune-sensitized cats.
AUTHOR: Padrid Philip A(a); Mitchell Richard W(a); Mdukwu I M(a); Spaethe Stephen; Shiou Peter; Cozzi Phillip(a); Leff Alan R
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JOURNAL: American Journal of Veterinary Research 56 (1):p109-115 1995
ISSN: 0002-9645
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We assessed the effect of serotonergic inhibition by cyproheptadine on the responsiveness of tracheal smooth muscle (TSM) strips and epithelium-intact third-generation bronchial rings from

immune-sensitized (Ascaris suum) cats after exposure to antigen. Cats were sensitized by IM administration of antigen and adjuvant twice over a 4-week period. Sensitization was confirmed in vivo by skin testing with antigen and by physiologic airway responses after exposure to %%%nebulized%%% antigen. Tissues were tethered isometrically to force transducers and were actively equilibrated by exposures to KCl-substituted perfusate. Maximal response after exposure to antigen (expressed as percentage of maximal contraction of each tissue to 63 mM KCl (%KCl) was 169 +- 18% KCl for sensitized TSM and 43 +- 18% KCl for sensitized TSM pretreated with cyproheptadine (P lt 0.001). Similarly, maximal response to antigen was 81 +- 27% KCl for sensitized bronchial rings, compared with 16 +- 14% KCl for sensitized bronchial rings pretreated with cyproheptadine (P = 0.05 vs control). Blockade of %%%leukotriene%%% synthesis by 10-6 to 10-4 M A-64077, a selective 5-lipoxygenase inhibitor, had no significant effect on peak response for either TSM (193 +- 13% KCl vs 169 +- 18% KCl for sensitized untreated TSM) or bronchial rings (79 +- 20% KCl vs 81 27% KCl for sensitized untreated bronchial rings). Release of serotonin from airway tissues was confirmed by the presence of serotonin in the perfusate of 8 sensitized TSM preparations after, but not before, antigen challenge. Our data indicate that airways from immune-sensitized cats have typical immediate-type hypersensitivity responses when exposed to antigen and that these responses are inhibited by serotonin-receptor blockade, but not by blockade of 5-lipoxygenase. These data implicate serotonin as an important mediator in the immediate-type hypersensitivity reaction in the immune-sensitized airways of cats and suggest a potential role for serotonin antagonists in the clinical treatment of asthma in this species.

09461556 BIOSIS NO.: 199497469926
Antigen-induced airway responses are inhibited by a potassium channel opener.
AUTHOR: Ichinose Masakazu; Miura Motohiko; Takahashi Tsuneyuki; Yamauchi Hideyuki; Nakajima Natsuko; Igarashi Atsushi; Ishikawa Jun; Inoue Hiroshi ; Maeyama Kazutaka; et al
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JOURNAL: American Journal of Respiratory and Critical Care Medicine 150 (2):p388-393 1994
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have investigated the effect of a potassium channel opener, BRL 38227, on antigen-induced bronchoconstriction and airway microvascular leakage in sensitized guinea pigs by simultaneously measuring pulmonary resistance (RL) and extravasation of Evans blue dye. Guinea pigs were sensitized 3 wk before experimentation with ovalbumin (OA) and aluminum hydroxide. The trachea was cannulated, and lungs were mechanically ventilated. All animals were pretreated 30 min before experimentation with atropine (1 mg/kg intravenously) and propranolol 1 mg/kg to block muscarinic and beta-adrenergic responses, respectively. BRL 38227 (200 mu-g/kg) was administered intravenously 1 min before intravenous dye injection (30 mg/kg); OA (3 mg/ml) was inhaled using an ultrasonic %%%nebulizer%%% (for 30 s) 1 min after dye injection. BRL 38227 significantly inhibited OA-induced bronchoconstrictor response (p lt 0.01) and plasma leakage in trachea (p lt 0.05) and main bronchi (p lt 0.05). BRL 38227 also had an inhibitory effect on exogenous histamine- and %%%leukotriene%%%-induced bronchoconstriction and microvascular leakage. However, BAL 38227 did not affect OA-induced histamine release from minced lung tissues in sensitized guinea pigs. We conclude that the allergic bronchoconstrictor response and airway plasma leakage are inhibited by a potassium channel opener, possibly as a result of its effect on the airway smooth muscle and the postcapillary venule level.

14/7/12
DIALOG(R)File 5:Biosis Previews(R)

09139918 BIOSIS NO.: 199497148288
Analysis of differential cell counts of sputa induced by inhalation of ultrasonically nebulized hypertonic saline or distilled water in asthmatic patients.
AUTHOR: Matsuura Takayuki(a); Gonogami Yoshiki(a); Kurokawa Masatsugu(a); Horikoshi Shojirou(a); Tomita Ken(a); Noda Hiromichi(a); Matsukura Satoshi(a); Adachi Mitsuru(a); Tanaka Yuko
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JOURNAL: Japanese Journal of Allergology 42 (11):p1657-1669 1993
ISSN: 0021-4884
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Japanese; Non-English
SUMMARY LANGUAGE: Japanese; English

ABSTRACT: Bronchial asthma is an inflammatory disease of the airways, and a simple method of evaluating inflammation, safer than BALF or bronchial mucosal biopsy, has long been sought after. The induction of sputa by the inhalation of an appropriate solution and the examination of the induced sputa may provide such a method. We compared the safety of two sputum induction methods, ultrasonically %%%nebulized%%% hypertonic saline inhalation and distilled water inhalation, and examined the usefulness of differential cell counts of the induced sputa. The safety of these methods was ascertained by determining lung functions (FEV-1.0, PEFR) and urinary %%%leukotriene%%% E-4 before and after inhalation of these solutions, and the usefulness of differential cell counts of induced sputa by examining the uniformity/reproducibility. Only after the inhalation of distilled water did the lung function reveal a statistically significant decrease when the data were compared with the control values for each of the two methods (p lt 0.01), and when the data obtained with distilled water inhalation and hypertonic saline inhalation were compared (p lt 0.05). The urinary %%%leukotriene%%% E-4 levels obtained were not very different between the two methods; however, in two patients, urinary %%%leukotriene%%% E-4 levels were increased markedly only after inhalation of distilled water. The uniformity of the sputum differential cell counts in the same specimen (evaluated by intraclass correlation coefficient) and inter-specimens (evaluated by Friedman test) was satisfactory for both methods, except for basophils. Hypertonic saline inhalation at 24-hour intervals gave a better reproducibility in differential cell counts of the induced sputa (evaluated by intraclass correlation coefficient), when compared with distilled water inhalation. These results suggest that hypertonic saline inhalation is safer and more useful than distilled water inhalation for induction of sputum in a uniform and reproducible way, and that the induction of sputum by hypertonic saline inhalation will be clinically useful in asthmatic patients who cannot expectorate sputa spontaneously.

14/7/13
DIALOG(R)File 5:Biosis Previews(R)

08339353 BIOSIS NO.: 000094090601
RECOVERY OF LEUKOTRIENE E-4 FROM THE URINE OF PATIENTS WITH AIRWAY OBSTRUCTION
AUTHOR: DRAZEN J M; O'OBRIEN J; SPARROW D; WEISS S T; MARTINS M A; ISRAEL E ; FANTA C H
AUTHOR ADDRESS: COMBINED PROGRAM PULMONARY/CRITICAL CARE MED., C/O PROGRAM OFFICE, BRIGHAM WOMEN'S HOSP., 75 FRANCIS STREET, BOSTON, MASS. 02115.
JOURNAL: AM REV RESPIR DIS 146 (1). 1992. 104-108. 1992
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The urinary excretion of %%%leukotriene%%% E4 (LTE4) was measured

in subjects presenting for emergency treatment of airway obstruction. A total of 72 subjects presenting with airway obstruction performed peak flow determinations before and after three treatments with %%%nebulized%%% albuterol given at 20-min intervals. Of these subjects, 22 more than doubled their peak flow rates, while 19 failed to increase their peak flow rates more than 25% during the treatment period. These groups were designated "responders" and "nonresponders", respectively. Urinary LTE4 excretion was determined in 16 of the 22 responders and 12 of the 19 nonresponders as well as 13 normal subjects by precolumn extraction, analytic reversed-phase high-performance liquid chromatography, and enzyme immunoassay. In the normal subjects the urinary LTE4 excretion was significantly ($p < 0.0001$) less than the urinary LTE4 measured in the responder subjects, but not less than the urinary LTE4 excretion in the nonesponder group ($p = 0.071$). The enhanced recovery of LTE4 from the urine of subjects with acutely reversible airway narrowing is consistent with a bronchoconstrictor role for the cysteinyl leukotrienes in spontaneous acute asthma.

14/7/14
DIALOG(R)File 5:Biosis Previews(R)

08296561 BIOSIS NO.: 000094067859
THE EFFECTS OF LIPOXIN A-4 ON AIRWAY RESPONSES IN ASTHMATIC SUBJECTS
AUTHOR: CHRISTIE P E; SPUR B W; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY AND ALLIED RESPIRATORY DISORDERS, 4TH FLOOR, HUNTS' HOUSE, GUY'S HOSP., LONDON SW1 9RT, UK.
JOURNAL: AM REV RESPIR DIS 145 (6). 1992. 1281-1284. 1992
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This study was performed to determine whether lipoxin A4 (LXA4) inhalation in asthmatic subjects has an effect on airways response. Eight subjects (six asthmatic, two normal) attended for bronchial inhalation challenge with LXA4. In three of these subjects (two asthmatics, one normal) blood pressure, pulse, and symptoms before and after challenge were recorded. Subsequently five male patients with mild asthma (22 to 34 yr of age) reattended for bronchial inhalation challenge with either %%%leukotriene%%% C4 (LTC4) or the combination of LTC4 and 1 .times. 10-4 M LXA4. After inhalation of each dose of agonist SGaw and V25 were measured. Airway responsiveness was determined by the concentration of agonist in the %%%nebulizer%%% required to induce a 35% fall in SGaw (PC35). There was no effect of LXA4 inhalation of SGaw, V25, blood pressure, pulse, or symptoms. There was a significant shift of the SGaw and V25 dose-response curve to the right after inhalation challenge with LTC4 combined with 1 .times. 10-4 M LXA4 as compared with that after inhalation challenge with LTC4 alone ($p < 0.01$ and $p < 0.025$, respectively). Thus, LXA4 may modulate LTC4-induced airway obstruction and may act as an endogenous sulfidopeptide %%%leukotriene%%% receptor antagonist.

14/7/15
DIALOG(R)File 5:Biosis Previews(R)

07911966 BIOSIS NO.: 000093011089
INTERACTION OF THROMBOXANE A2 AND LEUKOTRIENES IN GUINEA-PIG AIRWAYS IN-VIVO
AUTHOR: FUJIMURA M; BANDO T; MIZUHASHI K; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV., SCH. MED., 13-1 TAKARA-MACHI, 920 KANAZAWA, JPN.
JOURNAL: PROSTAGLANDINS 42 (4). 1991. 379-389. 1991
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effects of a thromboxane A2 receptor antagonist (S-1452) on bronchoconstriction induced by inhaled %%%leukotriene%%% C4 and a %%%leukotriene%%% receptor antagonist (AS-35) on bronchoconstriction caused by inhalation of a thromboxane A2 mimetic (STA2) were studied in anesthetized, artificially ventilated guinea pigs in order to examine the interaction of thromboxane A2 and leukotrienes in airways. 0.01-1.0 .mu. g/ml of %%%leukotriene%%% C4 and 0.1-1.0 .mu. g/ml of STA 2 inhaled from ultrasonic %%%nebulizer%%% developed for small animals caused dose-dependent increase of pressure at the airway opening (Pao) which is considered to be an index representing bronchial response. Pretreatment of the animals with inhaled S-1452 (0.01,0.033 mg/ml) significantly reduced the airway responses produced by 0.01,0.033,0.1,0.33 and 1.0 .mu. g/ml of %%%leukotriene%%% C4 in a dose dependent manner, While pretreatment with inhaled AS-35 (1mg) did not affect the STA2 dose-response curve. These findings suggest that %%%leukotriene%%% C4 activates thromboxane A2 generation while thromboxane A2 does not influence 5-lipoxygenase pathway in the airways.

14/7/16
DIALOG(R)File 5:Biosis Previews(R)

07910042 BIOSIS NO.: 000093009165
INHIBITORY EFFECT OF INHALATION OF A THROMBOXANE SYNTHETASE INHIBITOR ON BRONCHOCONSTRICTION INDUCED BY AEROSOLIZED LEUKOTRIENE C-4 AND THROMBOXANE A-2 ANALOGUE IN ANESTHETIZED GUINEA-PIGS
AUTHOR: FUJIMURA M; OGAWA H; SAITO M; SAKAMOTO S; MIYAKE Y; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA 920, JPN.
JOURNAL: ALLERGY (CPH) 46 (7). 1991. 534-539. 1991
CODEN: LLRGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effect of aerosol administration of a thromboxane synthetase inhibitor (OKY-046) on bronchoconstriction induced by aerosol %%%leukotriene%%% C4, histamine and a thromboxane A2 analogue (STA2) was studied in anesthetized, artificially ventilated guinea pigs in order to evaluate the effectiveness of inhalation of OKY-046 on an unfavorable mechanism of secondary release of thromboxane A2. 0.01-1.0 .mu.g/ml %%%leukotriene%%% C4, 25-400 .mu.g/ml histamine and 0.033-1.0 .mu.g/ml STA2 inhaled from an ultrasonic %%%nebulizer%%% developed for small animals caused a dose-dependent increase of pressure at the airway opening (Pao), which is considered to be an index representing bronchial response. Pretreatment of the animals with aerosol OKY-046 (0.035 and 0.35 mg/animal) significantly reduced the airway responses produced by inhalation of %%%leukotriene%%% C4 and STA2, in a dose-dependent manner, while the pretreatment did not affect the histamine dose-response curve. These findings suggest that aerosol %%%leukotriene%%% C4 and STA2 activate thromboxane synthesis in the airway, and inhalation of OKY-046 may be useful for preventing the secondary release of thromboxane A2, which is an unfavorable mechanism in asthma.

14/7/17
DIALOG(R)File 5:Biosis Previews(R)

07892832 BIOSIS NO.: 000092142313
THE POTENT AND SELECTIVE SULFIDOPEPTIDE LEUKOTRIENE ANTAGONIST SKF-104353 INHIBITS ASPIRIN-INDUCED ASTHMA
AUTHOR: CHRISTIE P E; SMITH C M; LEE T H
AUTHOR ADDRESS: DEP. ALLERGY ALLIED RESPIRATORY DISORDERS, 4TH FLOOR, HUNT'S HOUSE, GUY'S HOSP., LONDON SE1 9RT, UK.
JOURNAL: AM REV RESPIR DIS 144 (4). 1991. 957-958. 1991
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have determined the effect of prior inhalation of the LTD4 antagonist SK&F 104353 on the response to aspirin ingestion in six aspirin-sensitive asthmatic subjects (five women and one man 31 to 54 yr of age) in a randomized, double-blind, cross-over, placebo-controlled study. Pretreatment with inhaled SK&F 104353 (average %%%nebulized%%% dose, 893 .mu.g) inhibited the response by a mean of 47% (p = 0.02). The inhibition was partial, ranging from 43 to 74% in five subjects. In the remaining subject, there was no effect on the drug on the asthmatic response. We conclude that the mechanism of aspirin-induced asthma is at least partially mediated by the leukotrienes in the majority of susceptible patients and that %%%leukotriene%%% antagonists may be useful in the treatment of aspirin-induced asthma.

14/7/18
DIALOG(R)File 5:Biosis Previews(R)

07890994 BIOSIS NO.: 000092140297
A NOVEL METHOD FOR THE EVALUATION OF BRONCHOACTIVE AGENTS IN THE CONSCIOUS GUINEA-PIG
AUTHOR: BALL D I; COLEMAN R A; HARTLEY R W; NEWBERRY A
AUTHOR ADDRESS: DEP. PERIPHERAL PHARMACOL., GLAXO GROUP RES. LTD., WARE, HERTS. SG12 0DP, UK.
JOURNAL: J PHARMACOL METHODS 26 (3). 1991. 187-202. 1991
FULL JOURNAL NAME: Journal of Pharmacological Methods
CODEN: JPMED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We describe a simple, noninvasive, nontraumatic and reproducible method in which the activities of bronchoactive agents may be recorded in six conscious guinea pigs simultaneously. The method involves the use of "head out" whole body plethysmographs from which respiratory rate can be recorded, by monitoring respiration-related changes in pressure within the body chamber. Exposure of a guinea pig to an aerosolized bronchoconstrictor agent causes an increase in respiratory rate, which is quantified by measuring the area under the respiratory rate curve using a purpose-built respiratory computer. This can be carried out for six animals simultaneously and independently. When exposed to a standard bronchoconstrictor aerosol challenge at intervals over a 6 hr period, the areas under the respiratory rate curves for each animal are highly reproducible. Inhalation of %%%nebulized%%% solutions of acetylcholine (ACh), histamine (Hist), 5-hydroxytryptamine, bradykinin, %%%leukotriene%%% D4 and the thromboxane A2-mimetic, U-46619, but not prostaglandin F2.alpha. (PGF2.alpha.) caused dose-related bronchoconstriction observed as increases in respiratory rate. In addition, salbutamol, clenbuterol, N-ethylcarboxamide adenosine (NECA) and PGE2 all inhibited ACh (1 mg mL-1) and Hist (1 mg mL-1)-induced increases in respiratory rate in a dose-related fashion. The method described, which is both noninvasive and nontraumatic, may therefore be used to quantify in the conscious guinea pig, both bronchoconstrictor and bronchodilator agents.

14/7/19
DIALOG(R)File 5:Biosis Previews(R)

07776836 BIOSIS NO.: 000092080207
PARTICIPATION OF THE CYSTEINYL LEUKOTRIENES IN THE ACUTE BRONCHOCONSTRICTOR RESPONSE TO INHALED PLATELET ACTIVATING FACTOR IN MAN
AUTHOR: SPENCER D A; EVANS J M; GREEN S E; PIPER P J; COSTELLO J F
AUTHOR ADDRESS: BIRMINGHAM CHILDRENS HOSP., BIRMINGHAM B16 8ET.
JOURNAL: THORAX 46 (6). 1991. 441-445. 1991
FULL JOURNAL NAME: Thorax
CODEN: THORA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: To determine whether the effects of platelet activating factor on

the airways may be due to the production of leukotrienes we studied the effects of pretreatment with the selective cysteinyl %%%leukotriene%%% antagonist SK&F 104353-Z2 on the airway and cellular responses to inhaled platelet activating factor. Eight healthy men were studied in a randomised, double blind placebo controlled crossover study. A single dose of platelet activating factor that caused a fall of at least 35% in specific airways conductance (sGaw) was determined initially for each subject. Challenge with this dose of platelet activating factor was then carried out on two further occasions after pretreatment with a single %%%nebulised%%% dose of SK&F 104353-Z2 or placebo. The % reudctions in specific airways conductance and of partial flow at 30% of vital capacity (P.ovrhdot.Vmax30) were less after SK&F 104353-Z2 than after placebo (22 versus 34 for sGaw, 19 versus 31 for P.ovrhdot.Vmax30). The mean (95% confidence limits (CL)) differences in the maximum % fall from control values for SK&F 104353-Z2 and placebo were -12.6 (-23.8, -1.4) for sGaw and -12.5, (-20.8 -4.2) for P.ovrhdot.Vmax30. The mean % fall in neutrophil count was similar after SK&F 10453-Z2 (46%) and after placebo (50%) (95% CL of difference 13.6, 6.6). Bronchial responsiveness to methacholine did not increase above baseline values in any subject when measured two weeks after challenge by platelet activating factor. This study suggests that leukotrienes play a part in the response to platelet activating factor in man.

14/7/20
DIALOG(R)File 5:Biosis Previews(R)

07437272 BIOSIS NO.: 000091043261
THE EFFECT OF LEUKOTRIENE B-4 INHALATION ON AIRWAY RESPONSIVENESS IN DOGS
AUTHOR: IMAI T; NAMBU F; ADACHI M; TAKAHASHI T; SAITO C; MAEDA M; TSUJI A
AUTHOR ADDRESS: THE FIRST DEP. INTERNAL MED., SCH. MED., SHOWA UNIVERSITY, JAPAN.
JOURNAL: JPN J ALLERGOL 39 (10). 1990. 1380-1387. 1990
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: We studied the effect of %%%leukotriene%%% B4 (LTB4) inhalation on airway responsiveness in 12 dogs. LTB4 (10 .mu.g/ml) was delivered as an aerosol, generated from a Devilbiss 646 %%%nebulizer%%% for ten minutes. Airway responsiveness to inhaled methacholine was determined by modified Astograph (7 Hz oscillation method) 1 hr (n = 6) and 6 hr (n = 6) after LTB4 inhalation. After measurement of airway responsiveness, total cell counts, differential cell counts, thromboxane B2 (TxB2) and 6-keto-prostaglandin (PG)F1.alpha. levels in bronchoalveolar lavage fluid (BALF) were measured. The total cell counts in BALF increased after LTB4 inhalation ($p < 0.05$), and the neutrophil counts in BALF increased significantly 1 hr ($p < 0.05$) and 6 hr after ($p < 0.01$) LTB4 inhalation. Airway responsiveness to inhaled methacholine decreased significantly 1 hr ($p < 0.05$) and 6 hr ($p < 0.01$) after LTB4 inhalation. There were no significant changes in the levels of TxB2 or 6-keto-PGF1.alpha. in BALF 1 hr and 6 hr after LTB4 inhalation. These results suggest that inhaled LTB4 causes neutrophil recruitment into the airway but does not increase airway responsiveness to inhaled methacholine, and the possibility that LTB4 reduces airway responsiveness to inhaled methacholine exists in dogs.

14/7/21
DIALOG(R)File 5:Biosis Previews(R)

07404699 BIOSIS NO.: 000091020309
IGG-1-MEDIATED ACUTE PULMONARY HYPERSENSITIVITY RESPONSE IN THE GUINEA-PIG INVOLVEMENT OF SPECIFIC LIPID MEDIATORS
AUTHOR: WATSON J W; CONKLYN M; SHOWELL H J
AUTHOR ADDRESS: DEP. IMMUNOLOGY INFECTIOUS DISEASES, CENTRAL RESEARCH DIVISION, PFIZER INC., GROTON, CONN. 06340.
JOURNAL: AM REV RESPIR DIS 142 (5). 1990. 1093-1098. 1990

FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We determined the pulmonary obstructive response to aerosolized antigen challenge, and its sensitivity to antagonists of specific lipid mediators, in IgG1 passively sensitized (IgG1-PS) guinea pigs. Antiovalbumin (OA)-IgG1 was isolated by affinity chromatography from serum derived from actively immunized Hartley guinea pigs. Propranolol and pyrilamine pretreated, IgG1-PS guinea pigs were challenged with aerosolized antigen and pulmonary obstruction was quantified by measurements of excised lung gas volume (ELGV). ELGV increased between 150 and 1,035% in a dose-proportional fashion with increasing antigen exposure (0.001 to 0.1% %%%nebulizer%%% concentration). The %%%leukotriene%%% antagonists ICI-204,219 and SKF-104,353 exhibited dose-proportional inhibitions in antigen-induced elevations in ELGV, inhibiting up to 65 and 87% at the maximal concentrations examined. Similarly, the platelet-activating factor (PAF) antagonists WEB-2086 and L-659,989 inhibited antigen-induced elevations in ELGV, inhibiting up to 94 and 59% at the maximal concentrations examined. In contrast, the cyclooxygenase (CO) inhibitor piroxicam significantly enhanced ($p < 0.05$) the OA-induced elevations in ELGV. Aerosolized PAF challenge produced dose-proportional elevations in ELGV that were significantly inhibited by the LTD4 antagonist ICI-204,219 (38 and 43% inhibition) and the CO inhibitor piroxicam (62 and 48% inhibition) in sensitized and nonsensitized animals, respectively. We hypothesize that IgG1-dependent airway obstruction is mediated in part by LTD4 produced in response to PAF generation.

14/7/22
DIALOG(R)File 5:Biosis Previews(R)

06760215 BIOSIS NO.: 000088069648
EVIDENCE OF PAF-ACETHER METABOLIC PATHWAY ACTIVATION IN ANTIGEN CHALLENGE OF UPPER RESPIRATORY AIRWAYS
AUTHOR: MIADONNA A; TEDESCHI A; ARNOUX B; SALA A; ZANUSSI C; BENVENISTE J
AUTHOR ADDRESS: VIA COL MOSCHIN 1, 20136 MILAN, ITALY.
JOURNAL: AM REV RESPIR DIS 140 (1). 1989. 142-147. 1989
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Lyso-PAF-acether and PAF-acether (formerly platelet-activating factor) were detected in nasal secretions from patients with hay fever who underwent local antigen challenge. Lyso-PAF release was observed in 12 of 13 patients, with a maximum ($p < 0.001$) 5 min after stimulation and a progressive decrease during the first hour. PAF was detected in the 5-min postchallenge nasal washings from two of 13 subjects. After HPLC, this mediator was found in four of seven postchallenge nasal washings submitted to this procedure, with a peak 5 min and 10 min after provocation. Histamine analysis revealed a significant ($p < 0.001$) but time-limited (5 min) release in nasal secretion. The pattern of immunoreactive %%%leukotriene%%% C4 showed a maximal peak ($p < 0.01$) 5 min after allergen provocation, with raised levels for 20 min. Nasal stimulation with %%%nebulized%%% saline solution or grass pollens in healthy subjects and in patients suffering from allergic rhinitis caused by Dermatophagoides pteronyssinus was followed by no local mediator release. These data indicate that, in addition to histamine and peptide-leukotrienes, lyso-PAF and PAF are released in nasal secretions after local antigen stimulation in patients with hay fever, with a preponderance of lyso-PAF response. On the basis of these results, it is conceivable that these ether-phospholipids may be involved in allergic inflammation of human nasal airways.

14/7/23
DIALOG(R)File 5:Biosis Previews(R)

06756813 BIOSIS NO.: 000088066246
PREVENTION AND REVERSAL OF AEROSOL LTD-4-INDUCED CHANGES IN GUINEA-PIG PULMONARY MECHANICS BY WY-48252 AN ORALLY ACTIVE LTD-4-E-4 RECEPTOR ANTAGONIST
AUTHOR: HAND J M; AUEN M A; CHANG J; ENGLEBACH I M
AUTHOR ADDRESS: SMITH KLINE AND FRENCH LAB., L-532, P.O. BOX 1539, KING OF PRUSSIA, PA. 19406-0939.
JOURNAL: INT ARCH ALLERGY APPL IMMUNOL 89 (1). 1989. 78-82. 1989
FULL JOURNAL NAME: International Archives of Allergy and Applied Immunology
CODEN: IAAAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Anesthetized male albino guinea pigs were prepared for recording changes in the pulmonary mechanics parameters, dynamic compliance (Cdyn) and airway conductance (Gaw). Two aerosol %%%leukotriene%%% D4 (LTD4) challenges (0.125 .mu.g/ml, 3-7 breaths, 1 h apart) were administered via an ultrasonic %%%nebulizer%%% to each animals and, produced reductions in Cdyn. Intraduodenal administration of the LTD4/E4 receptor antagonists Wy-48252 (30 min), Wy-45911 and Ly-171883 (15 min) produced dose-related inhibition of the second LTD4 challenge. From the data, ID50 values were calculated and, Wy 48252 was 8- to 17-fold more potent (mg/kg) than Wy-45911 or Ly-171883. Responses to histamine were not altered by the antagonists. In separate experiments, Wy-48252 (0.3 and 1 mg/kg i.v.) rapidly reversed aerosol LTD4-induced decreases of Cdyn and Gaw, but did not reverse pulmonary mechanics decreases produced by prostaglandin F2.alpha.. The results indicate that systemically administered LTD4 receptor antagonists can both prevent and reverse bronchoconstriction produced by aerosol LTD4 in the guinea pig.

14/7/24
DIALOG(R)File 5:Biosis Previews(R)

06185426 BIOSIS NO.: 000086019608
CONSCIOUS GUINEA-PIG AEROSOL MODEL FOR EVALUATION OF PEPTIDE LEUKOTRIENE ANTAGONISTS
AUTHOR: SNYDER D W; LIBERATI N J; MCCARTHY M M
AUTHOR ADDRESS: PULM. RES. GROUP, ELI LILLY CO., LILLY RES. LAB., MC 931, BUILD. 98/C/4, INDIANAPOLIS, INDIANA 46285.
JOURNAL: J PHARMACOL METHODS 19 (3). 1988. 219-232. 1988
FULL JOURNAL NAME: Journal of Pharmacological Methods
CODEN: JPMED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A new conscious animal model for evaluating %%%leukotriene%%% antagonists is described. The model consists of monitoring the change in the respiratory pattern induced by aerosol administration of various airway constrictors in six guinea pigs secured in a plexiglass chamber by a neck yoke. The animals are pretreated with indomethacin (10 mg/kg, i.p.) and propranolol (5 mg/kg, i.p.) 30 min prior to the challenge. After a 30-min stabilization period, the animals are challenged by various agonists delivered via a Monaghan ultrasonic %%%nebulizer%%% at a flow rate of 2.0 L/min for 5 min. The end point is defined as the onset of slow, labored abdominal breathing (dyspnea) measured in seconds. Peptide leukotrienes (LTs) (30 nM-60 .mu.M) produced concentration-related decreases in time to dyspnea with a rank order of potency of LTD4 > LTC4 > LTE4. LTD4 was 1,000-fold more potent than histamine or carbachol. Pretreatment of the animals with either FPL55712 or LY171883 delayed the time to reach dyspnea induced by LTD4. In contrast, pyrilamine, cyproheptadine, and phenoxybenzamine failed to alter LTD4-induced dyspnea. The results indicate that this model is useful in assessing the efficacy of LT receptor antagonists in vivo.

14/7/25
DIALOG(R)File 5:Biosis Previews(R)

06166028 BIOSIS NO.: 000086000210
SECONDARY RELEASE OF THROMBOXANE A2 IN AEROSOL LEUKOTRIENE C4-INDUCED BRONCHOCONSTRICTION IN GUINEA-PIGS
AUTHOR: FUJIMURA M; MIYAKE Y; UOTANI K; KANAMORI K; MATSUDA T
AUTHOR ADDRESS: THIRD DEP. INTERN. MED., KANAZAWA UNIV. SCH. MED., 13-1 TAKARA-MACHI, KANAZAWA, JPN.
JOURNAL: PROSTAGLANDINS 35 (3). 1988. 427-436. 1988
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Effect of a thromboxane synthetase inhibitor (OKY-046) on bronchconstriction induced by aerosol %%%leukotriene%%% C4 and histamine was studied in anesthetized, artificially ventilated guinea pigs in order to examine whether secondary release of thromboxane A2 is produced by aerosol %%%leukotriene%%% C4 or not. 0.01-1.0.mu.g/ml of %%%leukotriene%%% C4 and 12.5-400 .mu.g/ml of histamine inhaled from ultrasonic %%%nebulizer%%% developed for small animals caused dose-dependent increase of pressure at airway opening (Pao) which is considered to be an index representing bronchial response. Pretreatment of the animals with intravenous OKY-046 (100mg/kg) significantly reduced the airway responses produced by inhalation of 0.1, 0.33 and 1.0.mu.g/ml of %%%leukotriene%%% C4, while the pretreatment did not affect the histamine dose-response curve. Based on these findings and previous reports (6,7), it is suggested that aerosol %%%leukotriene%%% C4 activates arachidonate cyclooxygenase pathway including thromboxane A2 synthesis and the released cyclooxygenase products have a bronchodilating effect as a whole.

14/7/26
DIALOG(R)File 5:Biosis Previews(R)

06080575 BIOSIS NO.: 000085043724
BRONCHIAL RESPONSIVENESS TO INHALED LEUKOTRIENE D-4 IN BRONCHIAL ASTHMA
AUTHOR: YAMAI T; FUKUDA T; MAKINO S
AUTHOR ADDRESS: DEP. MED. CLINICAL IMMUNOL., DOKKYO UNIV. SCH. MED.
JOURNAL: JPN J ALLERGOL 36 (9). 1987. 838-847. 1987
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: In order to determine the role of %%%leukotriene%%% (LT) in bronchoconstriction in asthmatic patients, we compared the bronchial responsiveness to LTD4 of seven normal subjects and twenty six asthmatic subjects, and this was compared with the responsiveness to acetylcholine and histamine in the same asthmatic subjects. We carried out the LTD4 inhalation test using siliconized glass %%%nebulizers%%%, with the inhalation of 1 ml solution of an increasing concentration. Acetylcholiae and histamine inhalation test were carried out according to the standard method. Bronchial responsiveness was expressed as the cumulative dose or number of units causing a 20% fall in FEV1.0 (PD20), where one unit is defined as the inhalation of 1 .mu.g/ml solution of acetylcholine or histamine for 1 minute. The inhalation of 20000 ng of LTD4 did not decrease FEV1.0 by more than 20% in any of the normal subjects, but decreased it by 11.3 .+-. 5.1% (mean .+-. SD). In the asthmatic subjects PD20-LTD4 ranged from 30 ng to 14990 ng with a mean of 562 ng. The bronchi of the asthmatic subjects were over 40 times more sensitive to LTD4 than those of the normal subjects. There is statistically significant correlation between PD20-LTD4 and PD20-Ach ($r=0.690$, $p < 0.001$), PD20-LTD4 and PD20-Hist ($r=0.628$, $p < 0.001$). In addition LTD4 has an approximately 200 times more potent bronchoconstrictive effect in asthmatic patients than histamine and 700 times more than acetylcholine. Furthermore, patients with more severe asthmatic symptoms tend to have lower PD20-LTD4 than patients with milder symptoms. These results suggest that LTD4 has an important role in the bronchoconstriction of asthmatic

patients.

14/7/27
DIALOG(R)File 5:Biosis Previews(R)

06058752 BIOSIS NO.: 000085021901
THE EXCRETION OF LEUKOTRIENE E-4 INTO URINE FOLLOWING INHALATION OF LEUKOTRIENE D-4 BY HUMAN INDIVIDUALS
AUTHOR: VERHAGEN J; BEL E H; KIJNE G M; STERK P J; BRUYNZEEL P L B; VELDINK G A; VLIEGENTHART J F G
AUTHOR ADDRESS: DEP. BIO-ORGANIC CHEMISTRY, STATE UNIV. UTRECHT, PADUALAAN 8, NL-3584 CH UTRECHT, THE NETHERLANDS.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 148 (2). 1987. 864-868. 1987
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Healthy volunteers underwent bronchial challenge with increasing doses of %%%nebulized%%% %%%leukotriene%%% D4 (0.007-200 nmol) at 15 min intervals. Total amounts of 200 nmol (females) and 400 nmol (males) were inhaled, corresponding to approximately 100 nmol and 200 nmol deposited in the lung, respectively. Of the latter amounts 3 .+-. 1% (mean .+-. S.E.M., n=5) was found to be excreted as %%%leukotriene%%% E4 into the urine within 12 h. No further excretion after this period was observed. Approximately 50% of the total urinary %%%leukotriene%%% E4 was excreted during the first 2 h. These results suggest that a possible formation of sulfidopeptide leukotrienes in the lung in vivo can be monitored by measuring %%%leukotriene%%% E4 excretion into the urine.

14/7/28
DIALOG(R)File 5:Biosis Previews(R)

05735120 BIOSIS NO.: 000084083526
NEBULIZATION AND SELECTIVE DEPOSITION OF LTD-4 IN HUMAN LUNGS
AUTHOR: BISGAARD H; POULSEN L; SONDERGAARD I
AUTHOR ADDRESS: VESTER SOGADE 187, DK-1601 COPENHAGEN, DEN.
JOURNAL: ALLERGY (COPENH) 42 (5). 1987. 336-342. 1987
FULL JOURNAL NAME: ALLERGY (Copenhagen)
CODEN: LLRGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The process of %%%nebulization%%% and deposition of LTD4 was studied in detail. The concentration of LTD4 in a saline solution decreased by approximately 90% after 2 min of %%%nebulization%%% in a DeVilbiss 35B ultrasonic %%%nebulizer%%%. This decrease was prevented by diluting LTD4 in a phosphate buffer, pH 7.4. %%%Nebulization%%% of tritiated LTD4 in this phosphate buffer did not cause any appreciable deterioration of the %%%leukotriene%%%, as demonstrated by an unchanged ratio between radioactivity and LTD4 concentration in the test solution before and after %%%nebulization%%% as well as in the condensed aerosol. The aerosol generated by the DeVilbiss 35B ultrasonic %%%nebulizer%%% was shown to generate particles with a mass median diameter of 1.3 microns (dry particle size). Interposition of a settling bag reduced the amount of large particles, reducing the mass median diameter to 0.84 microns (dry particle size). Nine healthy volunteers were challenged on separate days with 40 nmol LTD4 or 100 .mu.mol histamine, and the changes in FEV1 and partial flow volume curves initiated at 50% of vital capacity (Vmax30) were measured. A relative diffuse deposition pattern was ensured by inhalation via a settling bag. These results were compared to challenges with a relatively central deposition pattern as ensured by inhalation directly from the %%%nebulizer%%% with brisk inhalation maneuvers. The diffuse deposition pattern caused minimal changes in FEV1 but pronounced effect in vmax30. The effects of LTD4 and histamine on FEV1 and Vmax30 changed in parallel when the deposition of the mediators was changed to a more central pattern. This indicates that the two

mediators do not differ with respect to any selective effects on different parts of the airways.

14/7/29
DIALOG(R)File 5:Biosis Previews(R)

04340642 BIOSIS NO.: 000078070186
PHARMACOLOGIC PROPERTIES OF FPL-55712 SODIUM 7-3-4 ACETYL-3-HYDROXY-2-PROPYLPHENOXYL-2-HYDROXYPROPOXY-4-OXO-8-PROPYL-4H-1 BENZOPYRAN-2-CARBOXYLATE ADMINISTERED BY AEROSOL
AUTHOR: O'DONNELL M; WELTON A F
AUTHOR ADDRESS: DEP. PHARMACOL. II, HOFFMANN-LA ROCHE INC., NUTLEY, N.J. 07110, USA.
JOURNAL: AGENTS ACTIONS 14 (1). 1984. 43-48. 1984
FULL JOURNAL NAME: Agents and Actions
CODEN: AGACB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: FPL 55712 was investigated by the aerosol route of administration for efficacy at protecting against %%%leukotriene%%%-induced bronchoconstrictions in guinea pigs and for mediator release inhibitory activity in passively sensitized rats. In the studies to investigate %%%leukotriene%%% antagonism, anesthetized, spontaneously breathing guinea pigs were pretreated with propranolol and were exposed via tracheal cannula to aerosols generated by a Monaghan %%%nebulizer%%%. Subsequently, the animals were artificially ventilated and challenged with LTD4 [%%%leukotriene%%% D4] or LTE4 (25 .mu.g/kg, i.v.). FPL 55712 produced a concentration-dependent inhibition of LTD4 and LTE4-induced bronchoconstriction (IC50 [median inhibitory concentration] 0.5% and 0.8%, respectively). Although the biologic half-life of FPL 55712, administered i.v., was very short (1.7 min against LTD4 and 1.2 min against LTE4) after aerosol administration the biological half-life was surprisingly long (120 min against LTD4 and 90 min against LTE4). Aerosolized FPL 55712 also possessed weak antiallergic activity in comparison to disodium cromoglycate when measured as an inhibitor of IgE-mediated anaphylactic bronchoconstriction in rats (IC50 of 2.0% and 0.01%, respectively). When administered by aerosol, FPL 55712 is evidently effective at protecting against %%%leukotriene%%%-induced bronchoconstrictions, exhibits a long duration of action and also possesses weak antiallergic activity.

14/7/30
DIALOG(R)File 5:Biosis Previews(R)

04222374 BIOSIS NO.: 000077048419
INDOMETHACIN POTENTIATES THE PULMONARY RESPONSE TO AEROSOL LEUKOTRIENE C-4 IN THE GUINEA-PIG
AUTHOR: LEITCH A G; COREY E J; AUSTEN K F; DRAZEN J M
AUTHOR ADDRESS: HARV. SCH. PUBLIC HEALTH, 665 HUNTINGTON AVE., BOSTON, MASS. 02115.
JOURNAL: AM REV RESPIR DIS 128 (4). 1983. 639-643. 1983
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Aerosol administration of %%%leukotriene%%% (LT) C4 to anesthetized, mechanically ventilated guinea pigs results in significant dose-dependent decrements in dynamic compliance (Cdyn) and pulmonary conductance (GL) when the concentration of LTC4 in the %%%nebulizer%%% is in the range of 0.5-5 .mu.g/ml. Pretreatment with indomethacin 30 mg/kg given. i.p. significantly potentiates the decrements in Cdyn and GL elicited by aerosol LTC4 at 1 .mu.g/ml. Potentiation of the pulmonary response is seen even with an aerosol LTC4 concentration of 0.3 .mu.g/ml, which alone produces only minimal changes in pulmonary mechanics in control animals. Bronchodilator prostaglandins are apparently important

inhibitory modulators of this pulmonary response and secondary thromboxane release probably does not contribute to the response to inhaled LTC4. The effect of indomethacin pretreatment in augmenting the pulmonary response to aerosol LTC4 in the guinea pig may have relevance for the phenomenon of asthma induced in humans by ingestion of nonsteroidal anti-inflammatory agents.

14/7/31
DIALOG(R)File 5:Biosis Previews(R)

04211832 BIOSIS NO.: 000077037877
INHIBITORY EFFECTS OF STEROIDS ON SLOW REACTING SUBSTANCE OF ANAPHYLAXIS MEDIATED BRONCHO CONSTRICTION IN THE GUINEA-PIG IN-VIVO EVALUATION WITH INHALATION OF ANTIGEN AND LEUKOTRIENE C-4
AUTHOR: FUJIMURA M
AUTHOR ADDRESS: THIRD DEP. INTERNAL MED., KANAZAWA UNIV., SCH. MED.
JOURNAL: JPN J ALLERGOL 32 (7). 1983. 365-375. 1983
FULL JOURNAL NAME: Japanese Journal of Allergology
CODEN: ARERA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Steroids are widely used in the treatment of bronchial asthma. In vitro experiments demonstrate that steroids inhibit synthesis of slow-reacting substance of anaphylaxis (SRS-A) from arachidonic acid. Using a recently developed %%%nebulizer%%%, the inhibitory effects of steroids on SRS-A mediated bronchoconstriction induced by inhalation of %%%leukotriene%%% C4 and antigen was studied in vivo in passively sensitized guinea pigs. Mean pulmonary resistance (RL) and dynamic compliance (Cdyn) were measured for objective parameters at airway response. Dexamethasone phosphate (20 mg/kg) was i.p. administered 18-22 h before inhalation of antigen or %%%leukotriene%%% C4. This pretreatment inhibited the SRS-A mediated bronchoconstriction induced by antigen inhalation, but not that induced by %%%leukotriene%%% C4 inhalation. The inhibitory effects of steroids were more remarkable on Cdyn than EL, and also in the later phase than in the earlier phase after antigen inhalation. Steroids apparently inhibit synthesis and/or release of SRS-A, in particular in the peripheral airways, but do not directly block the action of SRS-A.

14/7/32
DIALOG(R)File 5:Biosis Previews(R)

03899219 BIOSIS NO.: 000075077292
DIFFERING MECHANISMS FOR LEUKOTRIENE D-4 INDUCED BRONCHO CONSTRICTION IN GUINEA-PIGS FOLLOWING INTRA VENOUS AND AEROSOL ADMINISTRATION
AUTHOR: HAMEL R; MASSON P; FORD-HUTCHINSON A W; JONES T R; BRUNET G; PIECHUTA H
AUTHOR ADDRESS: MERCK FROSST CAN. INC., PO BOX 1005, POINTE CLAIRE, DORVAL, QUEBEC H9R 4P8.
JOURNAL: PROSTAGLANDINS 24 (3). 1982. 419-432. 1982
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: **%%%Leukotriene%%% D4 (LTD4) when administered i.v. or by aerosol** to guinea pigs produced changes in pulmonary mechanics including a decrease in dynamic compliance and an increase in pulmonary resistance. The effects of i.v. LTD4 (0.5 .mu.g kg-1) were short lived and abolished by pretreatment of the animal with either cyclooxygenase inhibitors, a thromboxane synthetase inhibitor (OKY 1555) or a slow reacting substance of anaphylaxis antagonist (FPL 55712 [7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)-2-hydroxypropoxy]-4-oxo-8-propyl-4H-1-benzopyran-2-carboxylic acid monosodium salt]). Bronchoconstriction produced by the i.v. infusion of LTD4 at 0.5 .mu.g kg-1 may be due to the release of thromboxane A2. In animals treated with

indomethacin, LTD4 at higher doses (> 0.8 .mu.g kg-1) still elicited a bronchoconstriction which could be blocked by FPL 55712. %%%Nebulization%%% of 0.1-1.0 .mu.g of LTD4 into the lung produced prolonged changes in pulmonary mechanics which were inhibited by FPL 55712 and were potentiated by indomethacin. LTD4, when administered by aerosol, produced effects on the lung which were not mediated by cyclooxygenase products. Responses to %%%nebulized%%% rather than i.v. LTD4 in the guinea pig may more closely resemble those seen in human tissues.

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     $7.15  TELNET
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 6/7/1
DIALOG(R)File   5:Biosis Previews(R)
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6/7/2
DIALOG(R)File   5:Biosis Previews(R)
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10021353   BIOSIS NO.: 199598476271
Allergen-induced late-phase airways obstruction in the pig: Mediator
  release and eosinophil recruitment.
AUTHOR: Fornhem C(a); Kumlin M; Lundberg J M; Alving K
AUTHOR ADDRESS: (a)Div. Pharmacology, Dep. Physiology Pharmacology,
  Karolinska Inst., S-171 77 Stockholm**Sweden
JOURNAL: European Respiratory Journal  8 (7):p1100-1109 1995
ISSN: 0903-1936
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The aim of this study was to develop a novel model for studies of
  mediator mechanisms involved in the late asthmatic reaction in the lower
  airways, by using the sensitized pig. The release of histamine and
  cysteinyl-containing leukotrienes (cys-LTs), as well as the levels of
  inflammatory cells in blood and bronchoalveolar lavage fluid, were
  determined and their relationship to plasma cortisol levels and pulmonary
  airways obstruction was noted. Specific-pathogen free pigs were actively
  sensitized with Ascaris suum allergen, and one group of animals was
  treated with a cortisol-synthesis inhibitor (metyrapone) by constant
  intravenous infusion. Ascaris suum allergen was %%%nebulized%%% into the
  lower airways and total lung resistance, blood leucocyte count and
  urinary levels of methylhistamine and %%%leukotriene%%% %%%E%%%-4 (LTE-4)
  were followed for 8 h, whereafter bronchoalveolar lavage was performed
  for analysis of leucocytes. An increase in urinary methylhistamine and
  LTE-4 was seen during the acute allergic reaction in both groups of pigs.
  Metyrapone treatment prolonged the acute release of histamine, and this
  was seen together with a prolonged acute bronchoconstrictor response. In
  metyrapone-treated pigs, a continuous release over 8 h was seen for
  cys-LTs, but not for histamine. A late blood eosinophilia was also seen
  in metyrapone-treated animals, starting 4-6 h after allergen challenge.
  Late cys-LT release and eosmophilia were absent in non-metyrapone-treated
  animals. These results suggest that allergen-induced late release of
  cys-LTs as well as blood eosinophilia occur simultaneously with
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late-phase airways obstruction in the pig, and that all these reactions are prevented by high levels of endogenous cortisol.

6/7/3
DIALOG(R)File 5:Biosis Previews(R)

09139918 BIOSIS NO.: 199497148288
Analysis of differential cell counts of sputa induced by inhalation of ultrasonically %%%nebulized%%% hypertonic saline or distilled water in asthmatic patients.
AUTHOR: Matsuura Takayuki(a); Gonogami Yoshiki(a); Kurokawa Masatsugu(a); Horikoshi Shojirou(a); Tomita Ken(a); Noda Hiromichi(a); Matsukura Satoshi(a); Adachi Mitsuru(a); Tanaka Yuko
AUTHOR ADDRESS: (a)First Dep. Internal Med., Sch. Med., Showa Univ., Tokyo **Japan
JOURNAL: Japanese Journal of Allergology 42 (11):p1657-1669 1993
ISSN: 0021-4884
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Japanese; Non-English
SUMMARY LANGUAGE: Japanese; English

ABSTRACT: Bronchial asthma is an inflammatory disease of the airways, and a simple method of evaluating inflammation, safer than BALF or bronchial mucosal biopsy, has long been sought after. The induction of sputa by the inhalation of an appropriate solution and the examination of the induced sputa may provide such a method. We compared the safety of two sputum induction methods, ultrasonically %%%nebulized%%% hypertonic saline inhalation and distilled water inhalation, and examined the usefulness of differential cell counts of the induced sputa. The safety of these methods was ascertained by determining lung functions (FEV-1.0, PEFR) and urinary %%%leukotriene%%% %%%E%%%-4 before and after inhalation of these solutions, and the usefulness of differential cell counts of induced sputa by examining the uniformity/reproducibility. Only after the inhalation of distilled water did the lung function reveal a statistically significant decrease when the data were compared with the control values for each of the two methods (p lt 0.01), and when the data obtained with distilled water inhalation and hypertonic saline inhalation were compared (p lt 0.05). The urinary %%%leukotriene%%% %%%E%%%-4 levels obtained were not very different between the two methods; however, in two patients, urinary %%%leukotriene%%% %%%E%%%-4 levels were increased markedly only after inhalation of distilled water. The uniformity of the sputum differential cell counts in the same specimen (evaluated by intraclass correlation coefficient) and inter-specimens (evaluated by Friedman test) was satisfactory for both methods, except for basophils. Hypertonic saline inhalation at 24-hour intervals gave a better reproducibility in differential cell counts of the induced sputa (evaluated by intraclass correlation coefficient), when compared with distilled water inhalation. These results suggest that hypertonic saline inhalation is safer and more useful than distilled water inhalation for induction of sputum in a uniform and reproducible way, and that the induction of sputum by hypertonic saline inhalation will be clinically useful in asthmatic patients who cannot expectorate sputa spontaneously.

6/7/4
DIALOG(R)File 5:Biosis Previews(R)

08339353 BIOSIS NO.: 000094090601
RECOVERY OF %%%LEUKOTRIENE%%% %%%E%%%-4 FROM THE URINE OF PATIENTS WITH AIRWAY OBSTRUCTION
AUTHOR: DRAZEN J M; O'OBRIEN J; SPARROW D; WEISS S T; MARTINS M A; ISRAEL E ; FANTA C H
AUTHOR ADDRESS: COMBINED PROGRAM PULMONARY/CRITICAL CARE MED., C/O PROGRAM OFFICE, BRIGHAM WOMEN'S HOSP., 75 FRANCIS STREET, BOSTON, MASS. 02115.
JOURNAL: AM REV RESPIR DIS 146 (1). 1992. 104-108. 1992
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The urinary excretion of leukotriene E4 (LTE4) was measured in subjects presenting for emergency treatment of airway obstruction. A total of 72 subjects presenting with airway obstruction performed peak flow determinations before and after three treatments with %%%nebulized%%% albuterol given at 20-min intervals. Of these subjects, 22 more than doubled their peak flow rates, while 19 failed to increase their peak flow rates more than 25% during the treatment period. These groups were designated "responders" and "nonresponders", respectively. Urinary LTE4 excretion was determined in 16 of the 22 responders and 12 of the 19 nonresponders as well as 13 normal subjects by precolumn extraction, analytic reversed-phase high-performance liquid chromatography, and enzyme immunoassay. In the normal subjects the urinary LTE4 excretion was significantly ($p < 0.0001$) less than the urinary LTE4 measured in the responder subjects, but not less than the urinary LTE4 excretion in the nonresponder group ($p = 0.071$). The enhanced recovery of LTE4 from the urine of subjects with acutely reversible airway narrowing is consistent with a bronchoconstrictor role for the cysteinyl leukotrienes in spontaneous acute asthma.

6/7/5
DIALOG(R)File 5:Biosis Previews(R)

06058752 BIOSIS NO.: 000085021901
THE EXCRETION OF %%%LEUKOTRIENE%%% %%%E%%%-4 INTO URINE FOLLOWING INHALATION OF LEUKOTRIENE D-4 BY HUMAN INDIVIDUALS
AUTHOR: VERHAGEN J; BEL E H; KIJNE G M; STERK P J; BRUYNZEEL P L B; VELDINK G A; VLIEGENTHART J F G
AUTHOR ADDRESS: DEP. BIO-ORGANIC CHEMISTRY, STATE UNIV. UTRECHT, PADUALAAN 8, NL-3584 CH UTRECHT, THE NETHERLANDS.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 148 (2). 1987. 864-868. 1987
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Healthy volunteers underwent bronchial challenge with increasing doses of %%%nebulized%%% leukotriene D4 (0.007-200 nmol) at 15 min intervals. Total amounts of 200 nmol (females) and 400 nmol (males) were inhaled, corresponding to approximately 100 nmol and 200 nmol deposited in the lung, respectively. Of the latter amounts 3 .+. 1% (mean .+. S.E.M., n=5) was found to be excreted as leukotriene E4 into the urine within 12 h. No further excretion after this period was observed. Approximately 50% of the total urinary leukotriene E4 was excreted during the first 2 h. These results suggest that a possible formation of sulfidopeptide leukotrienes in the lung in vivo can be monitored by measuring leukotriene E4 excretion into the urine.

6/7/6
DIALOG(R)File 5:Biosis Previews(R)

06048489 BIOSIS NO.: 000085011638
THE EFFECT OF INHALED LEUKOTRIENE D-4 HISTAMINE OR ANTIGEN ON CENTRAL AND PERIPHERAL AIRWAYS OF GUINEA-PIGS ANALYSIS OF BRONCHOGRAMS WITH AN INTERACTIVE IMAGE ANALYSIS SYSTEM
AUTHOR: ASHIDA Y; NOMURA M; KURIKI H; MAKI Y
AUTHOR ADDRESS: BIOL. LAB., CENTRAL RES. DIV., TAKEDA CHEM. INDUSTRIES LTD., 17-85 JUSOHONMACHI 2-CHOME, YODOGAWA-KU, OSAKA 532, JPN.
JOURNAL: EUR J PHARMACOL 141 (2). 1987. 299-304. 1987
FULL JOURNAL NAME: European Journal of Pharmacology
CODEN: EJPHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of guinea pig airways of the inhalation of

leukotrienes, histamine or antigen was investigated by measuring changes in lung volume and analyzing the airway area on bronchograms with the Zeiss interactive image analysis system (IBAS). LTC4, LTD4, LTE4 and histamine inhaled through an ultrasonic %%%nebulizer%%% caused inflation of the lung: LTD4 was the most potent of the leukotrienes and was 100 times more potent than histamine on a molar basis. The results of analyses of areas of large and small bronchi and bronchioles on the bronchograms indicated that LTD4 selectively decreased the area of the peripheral airways. Inhalation of an antigen in actively sensitized animals resulted in inflation of the lung and in a selective decrease in the area of the peripheral airways. Anaphylactic bronchostriction provoked by antigen inhalation was clearly inhibited by AA-861, a 5-lipoxygenase inhibitor but not significantly by mepyramine, an antihistamine. These observations indicate that LTD4 is a potent constrictor of the peripheral airways in guinea pigs and that the anaphylactic bronchoconstriction provoked by antigen inhalation could be mediated by LTD4 in actively sensitized guinea pigs.

6/7/7
DIALOG(R)File 5:Biosis Previews(R)

04340642 BIOSIS NO.: 000078070186
PHARMACOLOGIC PROPERTIES OF FPL-55712 SODIUM 7-3-4 ACETYL-3-HYDROXY-2-PROPYLPHENOXYL-2-HYDROXYPROPOXY-4-OXO-8-PROPYL-4H-1 BENZOPYRAN-2-CARBOXYLATE ADMINISTERED BY AEROSOL
AUTHOR: O'DONNELL M; WELTON A F
AUTHOR ADDRESS: DEP. PHARMACOL. II, HOFFMANN-LA ROCHE INC., NUTLEY, N.J. 07110, USA.
JOURNAL: AGENTS ACTIONS 14 (1). 1984. 43-48. 1984
FULL JOURNAL NAME: Agents and Actions
CODEN: AGACB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: FPL 55712 was investigated by the aerosol route of administration for efficacy at protecting against leukotriene-induced bronchoconstrictions in guinea pigs and for mediator release inhibitory activity in passively sensitized rats. In the studies to investigate leukotriene antagonism, anesthetized, spontaneously breathing guinea pigs were pretreated with propranolol and were exposed via tracheal cannula to aerosols generated by a **Monaghan %%%nebulizer%%%. Subsequently, the animals were artificially ventilated and challenged with LTD4 [leukotriene D4] or LTE4 (25 .mu.g/kg, i.v.)**. FPL 55712 produced a concentration-dependent inhibition of LTD4 and LTE4-induced bronchoconstriction (IC50 [median inhibitory concentration] 0.5% and 0.8%, respectively). Although the biologic half-life of FPL 55712, administered i.v., was very short (1.7 min against LTD4 and 1.2 min against LTE4) after aerosol administration the biological half-life was surprisingly long (120 min against LTD4 and 90 min against LTE4). Aerosolized FPL 55712 also possessed weak antiallergic activity in comparison to disodium cromoglycate when measured as an inhibitor of IgE-mediated anaphylactic bronchoconstriction in rats (IC50 of 2.0% and 0.01%, respectively). When administered by aerosol, FPL 55712 is evidently effective at protecting against leukotriene-induced bronchoconstrictions, exhibits a long duration of action and also possesses weak antiallergic activity.

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DIALOG(R)File   5:Biosis Previews(R)
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12803233   BIOSIS NO.: 200100010382
Eicosanoid and muscarinic receptor blockade abolishes
  hyperventilation-induced bronchoconstriction.
AUTHOR: Freed Arthur N(a); McCulloch Sharron; Wang Yongqiang
AUTHOR ADDRESS: (a)School of Hygiene and Public Health, Johns Hopkins
  Univ., 615 North Wolfe St., Div., Rm. 7006, Baltimore, MD, 21205**USA
JOURNAL: Journal of Applied Physiology  89 (5):p1949-1955 November, 2000
MEDIUM: print
ISSN: 8750-7587
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: This study was designed to test the hypothesis that
  hyperventilation-induced bronchoconstriction (HIB) results from the
  combined effects of prostanoid and %%%leukotriene%%% metabolism. A
  %%%bronchoscope%%% was used in anesthetized dogs to record peripheral
  airway resistance and HIB before and after combined treatment with
  inhibitors of cyclooxygenase (indomethacin) and 5-lipoxygenase (MK-0591).
  Bronchoalveolar lavage fluid (BALF) cells and mediators from
  hyperventilated and control airways were also measured. Pretreatment with
  MK-0591 and indomethacin significantly attenuated, but did not abolish,
  HIB. However, addition of atropine nearly eliminated the residual
  response. Blockade of eicosanoid metabolism markedly reduced the
  concentrations of eicosanoids recovered in BALF after hyperventilation.
  Positive correlations between post-hyperventilation BALF prostanoid and
  epithelial cell concentrations are suggestive of mucosal injury-induced
  mediator production and release. We conclude that HIB is prevented in the
  presence of eicosanoid and muscarinic-receptor blockade and that both
  classes of eicosanoids contribute similarly to the development of HIB.


 9/7/2
DIALOG(R)File   5:Biosis Previews(R)
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12578714   BIOSIS NO.: 200000332216
Heparin inhibits eicosanoid metabolism and hyperventilation-induced
  bronchoconstriction in dogs.
AUTHOR: Suzuki Ryoichi; Freed Arthur N(a)
AUTHOR ADDRESS: (a)Division of Physiology, Johns Hopkins University, 615
  North Wolfe Street, 7006 SHPH, Baltimore, MD, 21205**USA
JOURNAL: American Journal of Respiratory and Critical Care Medicine  161 (6
):p1850-1854 June, 2000
MEDIUM: print
ISSN: 1073-449X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Inhalation of heparin, an anticoagulant, attenuates
  exercise-induced asthma (EIA) in human subjects. The purpose of this
  study was to determine if heparin inhibits hyperventilation-induced
  bronchoconstriction (HIB) in a canine model of EIA, and if its mode of
  action involves the inhibition of eicosanoid mediator production and
  release. We used a wedged %%%bronchoscope%%% technique to measure
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baseline peripheral airway resistance (Rp). We then performed either a 2-min or 5-min dry air challenge (DAC) by temporarily increasing from 200 to 2,000 ml/min the flow of 5% CO2 in air used to ventilate a wedged sublobar segment. We compared HIB before and 60 min after aerosol treatment with either bacteriostatic water (BW) or heparin. We found that (1) heparin had no effect on baseline Rp, (2) BW did not alter the response to DAC, and (3) heparin reduced HIB by apprx 50-60%. On the basis of bronchoalveolar lavage fluid (BALF) cell analysis, heparin and BW caused acute infiltration of macrophages and eosinophils, and heparin increased the number of erythrocytes recovered immediately after DAC. Despite these acute inflammatory effects initiated prior to DAC, BALF mediator analyses revealed that pretreatment with heparin either attenuated or abolished hyperventilation-induced %%%leukotriene%%%, prostaglandin, and thromboxane release. Thus, our data provide direct evidence that inhaled heparin inhibits eicosanoid mediator production and release caused by hyperventilation with dry air, and significantly attenuates HIB.

9/7/3
DIALOG(R)File 5:Biosis Previews(R)

07253867 BIOSIS NO.: 000090033743
DRY AIR-INDUCED LATE PHASE RESPONSES IN THE CANINE LUNG PERIPHERY
AUTHOR: FREED A N; ADKINSON N F JR
AUTHOR ADDRESS: DIV. OF PHYSIOL., 7006 HYGIENE, JOHNS HOPKINS UNIV., 615 NORTH WOLFE ST., BALTIMORE, MARYLAND 21205, USA.
JOURNAL: EUR RESPIR J 3 (4). 1990. 434-440. 1990
FULL JOURNAL NAME: European Respiratory Journal
CODEN: ERJOE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Although controversial, late phase responses in asthmatic subjects have been reported several hours after exercise. We previously showed that exposure to dry air increases collateral system resistance (Rcs) in the canine lung periphery, and produces acute airway responses analogous to those that characterize human exercise-induced asthma. We used a dual wedged %%%bronchoscope%%% technique in anaesthetized male mongrel dogs to monitor Rcs in: 1) control segments continuously exposed to 200 ml.cntdot.min-1 of 5% CO2 in air and 2) dry air challenged segments exposed to 2000 ml.cntdot.min-1 5% CO2 for 5 min. We examined Rcs at 5 min .apprx.5 h post-challenge in an attempt to document late phase airway obstruction. Five min after dry air challenge Rcs initially increased 114.+.SE 22%; contralateral control segments remained unchanged (n=9). Five hour post-challenge, Rcs in dry air segments was elevated 81.+.20% above pre-challenge baseline ($p<0.01$); contralateral control segments did not change significantly over the 5 h period. cell profile analyses of lavage samples at 5 hours revealed that neutrophils and eosinophils were significantly increased ($p<0.03$) in dry air challenged segments when compared to controls. %%%Leukotriene%%% C4/D4 concentration in lavage was correlated ($p<0.02$) with neutrophil infiltration. Thus, we conclude that the canine lung periphery represents a reproducible model of a dry air-induced late phase reaction.

9/7/4
DIALOG(R)File 5:Biosis Previews(R)

07165781 BIOSIS NO.: 000089032424
EFFECTS OF %%%LEUKOTRIENE%%% B-4 IN THE HUMAN LUNG RECRUITMENT OF NEUTROPHILS INTO THE ALVEOLAR SPACES WITHOUT A CHANGE IN PROTEIN PERMEABILITY
AUTHOR: MARTIN T R; PISTORESE B P; CHI E Y; GOODMAN R B; MATTHAY M A
AUTHOR ADDRESS: PULMONARY AND CRITICAL CARE MED., SEATTLE VETERANS ADMINISTRATION MED. CENT., 1660 S. COLUMBIAN WAY, SEATTLE, WASH. 98108.
JOURNAL: J CLIN INVEST 84 (5). 1989. 1609-1619. 1989
FULL JOURNAL NAME: Journal of Clinical Investigation
CODEN: JCINA

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Leukotriene%%% B4 (LTB4) is a major product of human alveolar macrophages and has potent chemotactic activity for neutrophils (PMN) in vitro. To evaluate the effects of LTB4 in the normal human lung, we instilled LTB4 (5 .times. 10-7M, 10 ml) into a subsegment of the right middle lobe and 0.9% NaCl (10 ml) into a subsegment of the lingula using a fiberoptic %%%bronchoscope%%% in 12 healthy human volunteers. 4 h later, we performed bronchoalveolar larvage of the same subsegments. Compared with the NaCl instillation, LTB4 caused a large increase in lavage total cells (NaCl = 6.8 .+. 1.0 .times. 106 vs. LTB4 = 26.4 .+. 5.0 .times. 106, P < 0.001), most of which were PMN (NaCl = 12.2 .+. 4.6% vs. LTB4 = 55.7 .+. 6.0%, P < 0.001). In contrast, there was only a small increase in lavage total protein, and the lavage total protein correlated weakly with lavage total cells and PMN. The production of superoxide anion by the lavage PMN in response to phorbol myristate acetate was similar to that of peripheral blood PMN. The migration of lavage PMN was normal toward the chemotactic peptide FMLP, but reduced toward LTB4 and zymosan-activated human serum. Morphometric analysis using transmission electron microscopy indicated a selective loss of small granules in the lung neutrophils as compared with peripheral blood neutrophils. The data indicate that in the normal human lung, LTB4 can recruit active PMN into the airspaces without causing a significant change in the protein permeability of the epithelial barrier.

9/7/5
DIALOG(R)File 5:Biosis Previews(R)

06722881 BIOSIS NO.: 000088032307
USE OF SEGMENTAL AIRWAY LAVAGE TO OBTAIN RELEVANT MEDIATORS FROM THE LUNGS OF ASTHMATIC AND CONTROL SUBJECTS
AUTHOR: ZEHR B B; CASALE T B; WOOD D; FLOERCHINGER C; RICHERSON H B; HUNNINGHAKE G W
AUTHOR ADDRESS: DEP. INTERNAL MED. C33-G, CH, UNIV. IOWA COLL. MED., IOWA CITY, IOWA 52242.
JOURNAL: CHEST 95 (5). 1989. 1059-1063. 1989
FULL JOURNAL NAME: Chest
CODEN: CHETB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Studies have demonstrated that increased amounts of histamine in the airways of asthmatic patients are associated with increased airway reactivity. However, using routine bronchoalveolar lavage (BAL), histamine can be detected in only a portion of asthmatic subjects and a minority of control populations. To obtain relevant mediators from the airways in higher concentrations by avoiding the dilution inherent with a standard BAL, a technique was developed to lavage isolated airway segments of the human lung that employed a double-lumen %%%bronchoscope%%% and a balloon-tipped catheter. Lavage fluid obtained by this method yielded significantly higher concentrations of histamine than that obtained with routine BAL (asthmatic subjects, 2,403 .+. 633 pg/ml vs 188 .+. 42 pg/ml; rhinitis subjects, 533 .+. 187 pg/ml vs 113 .+. 53 pg/ml; normal subjects, 174 .+. 63 pg/ml vs 11 .+. 11 pg/ml). Similar findings were also noted for prostaglandin D2 (PGD2). Segmental airway lavage also resulted in higher lavage fluid concentrations of LTB4 than routine BAL. Segmental airway lavage should help in studying the relationship of mast cell degranulation to airways reactivity in both asthmatic and other study populations.

9/7/6
DIALOG(R)File 5:Biosis Previews(R)

06285324 BIOSIS NO.: 000086119507
DIFFERENTIAL RESPONSES OF TISSUE VISCANCE AND COLLATERAL RESISTANCE TO HISTAMINE AND %%%LEUKOTRIENE%%% C-4

AUTHOR: LUDWIG M S; SHORE S A; FREDBERG J J; DRAZEN J M
AUTHOR ADDRESS: DEP. MED., BRIGHAM AND WOMEN'S HOSP., HARVARD MED. SCH., HARVARD SCH. PUBLIC HEALTH, BOSTON, MASS. 02115.
JOURNAL: J APPL PHYSIOL 65 (3). 1988. 1424-1429. 1988
FULL JOURNAL NAME: Journal of Applied Physiology
CODEN: JAPHE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alterations in tissue viscance (Vti) and collateral resistance (Rcoll) are both used as indexes of peripheral lung responses. However, it is not known whether the two responses reflect the effects of activation of the same contractile elements. We measured differential responses in Vti and Rcoll to histamine and %%%leukotriene%%% (LT) C4 to determine whether each evoked a similar pattern of response. Using the wedged %%%bronchoscope%%% constant-flow technique, we measured Rcoll in lobar segments of anesthetized, paralyzed, open-chest, mechanically ventilated mongrel dogs. In addition, we measured (with an alveolar capsule) alveolar pressure (PA) within the segment under study. This allowed us to calculate Vti, the component of the PA change in phase with segment flow. Rcoll and Vti measurements were obtained under base-line conditions and after local delivery of aerosols generated from histamine and LTC4. In five out of five lobes studied with both histamine and LTC4, the fractional Rcoll response to histamine was greater than the fractional Rcoll response to LTC4. In contrast, in four out of five lobes examined, the fractional increase in Vti accompanying the histamine response was less than the fractional increase in Vti accompanying LTC4 administration. These data suggest that anatomically distinct contractile elements influence Vti and Rcoll insofar as LTC4 and histamine evoke quantitatively different changes in these two indexes of peripheral lung responses.

9/7/7
DIALOG(R)File 5:Biosis Previews(R)

05429389 BIOSIS NO.: 000033030236
DIFFERENTIAL RESPONSES OF COLLATERAL RESISTANCE AND TISSUE VISCANCE TO HISTAMINE AND %%%LEUKOTRIENE%%% C-4
AUTHOR: LUDWIG M; SHORE S; FREDBERG J; DRAZEN J M
AUTHOR ADDRESS: HARVARD SCH. PUBLIC HEALTH, BRIGHAM AND WOMEN'S HOSP., BOSTON, MASS. 02115.
JOURNAL: JOINT ANNUAL MEETING OF THE AMERICAN LUNG ASSOCIATION AND THE AMERICAN THORACIC SOCIETY, NEW ORLEANS, LOUISIANA, USA, MAY 10-13, 1987. AM REV RESPIR DIS 135 (4 PART 2). 1987. A92. 1987
CODEN: ARDSB
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

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            5147  ENDOTRACHEAL
             606  S4
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? ds

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S4        606   LEUKOTRIENE()E
S5       6969   NEBUL?
S6          7   S4 AND S5
S7       1220   BRONCHOSCOPE
S8          0   S4 AND S7
S9          7   LEUKOTRIENE AND S7
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? s s11 and leukotriene
             129  S11
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? s intrathoracic
     S14   3496  INTRATHORACIC
? s leukotriene
     S15  14826  LEUKOTRIENE
? s s14 and s15
           3496  S14
          14826  S15
     S16      4  S14 AND S15
? t s16/7/1-4

 16/7/1
DIALOG(R)File   5:Biosis Previews(R)
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12836132   BIOSIS NO.: 200100043281
Urinary excretion of %%%leukotriene%%% E4 and eosinophil protein X in
  children with atopic asthma.
AUTHOR: Severien C(a); Artlich A; Jonas S; Becher G
AUTHOR ADDRESS: (a)Dept of Pediatrics, Children's Hospital Boeblingen,
  Bunsenstrasse 120, 71032, Boeblingen**Germany
JOURNAL: European Respiratory Journal  16 (4):p588-592 October, 2000
MEDIUM: print
ISSN: 0903-1936
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Measurement of %%%leukotriene%%% E4 (LTE4) in urine is a
  noninvasive method for assessing changes in the rate of total body
  cysteinyl %%%leukotriene%%% production. Eosinophil protein X (EPX) has
  been used to assess eosinophil activity and monitor inflammation in
  bronchial asthma. The aim of the study was to look for differences in
  urinary LTE4 and EPX concentrations between children with stable atopic
  asthma and healthy controls and to compare asthmatic children with
  different disease severity. In addition the relationship was evaluated
  between urinary LTE4 amd EPX levels and lung function. LTE4 was also
  measured (enzyme immunoassay) together with EPX (radio-immunoassay) in
  urine and lung function tests were carried out in children with mild
  asthma (steroid-naive) (n=49), moderate to severe asthma (using inhaled
  steroids) (n=31) and healthy control subjects (n=28). Urinary
  %%%leukotriene%%% E4 (LTE4) was significantly higher in children with
  asthma than in controls (median (25-75 percentile) 238.5 (126.5-375.7) SD
  191.8 versus 189 (51-253.2) SD 131.7 pgcntdotmg-1 creatinine; p=0.021).
  Urinary EPX was also significantly increased in asthmatic children
  compared with controls (85.5 (64-131.5) SD 76.2 versus 48.5 (43.2-90)
  112.1 mugcntdotmmol-1 creatinine; p=0.006). There were no differences in
  urinary LTE4 and EPX between the group of mild and the group of moderate
  to severe asthmatic children. There were significant associations between
  the urinary LTE4 and %%%intrathoracic%%% gas volume (ITGV), residual
  volume (RV), forced expiratory volume in one second (FEV1), forced
  expiratory capacity (FVC) and maximum expiratory flow rate at 25% of
  vital capacity (MEF25). Urinary EPX was only correlated with maximum
  expiratory flow rate at 75% of vital capacity (MEF75). Thus measurement
  of urinary LTE4 may predict the degree of airflow obstruction in
  asthmatic children. Urinary LTE4 and EPX are useful markers of airway
  inflammation and can be helpful in guiding asthma management. There was
  no correlation between LTE4 and EPX levels.


 16/7/2
DIALOG(R)File   5:Biosis Previews(R)
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09555185   BIOSIS NO.: 199598010103
Long-lasting inhibitory activity of the hetrazepinic BN 50730 on exudation
  and cellular alterations evoked by PAF and LPS.
```

AUTHOR: Pires Ana L A; Silva Patricia M R E; Pasquale Claudia; Castro-Faria-Neto Hugo C; Bozza Patricia T; Cordeiro Renato S B; Rae Giles A; Braquet Pierre; Lagente Vincent; Martins Marco A(a)
AUTHOR ADDRESS: (a)Dep. Fisiologia Farmacodinamica, Inst. Oswaldo Cruz FIOCRUZ, Av. Brasil 4365, 21045-900, C.P. 92**Brazil
JOURNAL: British Journal of Pharmacology 113 (3):p994-1000 1994
ISSN: 0007-1188
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: 1. Inhibitory effects of the hetrazepinic derivative BN 50730 on the rat pleural inflammatory response, triggered by PAF or lipopolysaccharides (LPS), were examined. The type of pharmacological blockade exerted by this antagonist in in vitro assays of eosinophil chemotaxis and platelet aggregation were also investigated. 2. %%%Intrathoracic%%% injection of PAF (1 mu-g per cavity) caused a 4 fold increase in the extravasated protein within 15 min and led to a marked eosinophil accumulation 24 h post-challenge. BN 50730 (0.5-10 mu-g per cavity) inhibited exudation by PAF dose-dependently without modifying the response induced by histamine, bradykinin or 5-hydroxytryptamine (5-HT). 3. The kinetics of the inhibitory effect on exudation revealed that the actions of WEB 2086 and BN 52021 (10 mu-g per cavity) were over within 2 and 4 h respectively, whereas BN 50730 (10 mu-g per cavity) retained 80% of its inhibitory activity for 4 days. 4. Oral treatment with BN 50730 (10-20 mg kg-1, 1 h beforehand) suppressed the leucocyte accumulation and late eosinophilia observed 6 and 24 h after PAF respectively, but did not modify the eosinophilia induced by %%%leukotriene%%% B-4 (LTB-4) or bradykinin. BN 50730 also failed to reduce the eosinophil accumulation induced by LPS but drastically inhibited the neutrophil influx. 5. The pre-incubation of rat peritoneal eosinophils for 10 min with BN 50730 (30 nM - 1 mu-M) dose-dependently inhibited the chemotaxis induced by PAF (0.1 mu-M) in vitro. The IC-50 values for BN 52021, WEB 2086 and BN 50730 in this system were 5, 5 and 0.05 mu-M respectively. 6. In separate assays, rat peritoneal eosinophils and rabbit washed platelets were preincubated with BN 50730 or WEB 2086 (1 mu-M) then subjected to a series of at least two consecutive washings in order to remove the antagonist from the receptor environment. Under such conditions, only the cells pretreated with WEB 2086 recovered the sensitivity to the lipid. 7. We conclude that BN 50730 is a potent, specific and long-acting PAF antagonist and its effect seems to result from a high affinity and non-competitive interaction of the drug with the PAF receptor.

16/7/3
DIALOG(R)File 5:Biosis Previews(R)

07612764 BIOSIS NO.: 000091130648
EOSINOPHIL ACCUMULATION IN THE RAT PLEURAL CAVITY AFTER MAST CELL STIMULATION WITH COMPOUND 48-80 INVOLVES PROTEIN SYNTHESIS AND IS SELECTIVELY SUPPRESSED BY DEXAMETHASONE
AUTHOR: MARTINS M A; PASQUALE C P; SILVA P M R E; CORDEIRO R S B; VARGAFTIG B B
AUTHOR ADDRESS: DEPARTAMENTO DE FISIOLOGIA E FARMACODINAMICA, INSTITUTO OSWALDO CRUZ, AVENIDA BRASIL 4365, CAIXA POSTAL 926, 20010 RIO DE JANEIRO, R.J., BRAZIL.
JOURNAL: INT ARCH ALLERGY APPL IMMUNOL 92 (4). 1990 (1991). 416-424. 1990 1991
FULL JOURNAL NAME: International Archives of Allergy and Applied Immunology
CODEN: IAAAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alterations in the local mast cell population and the eosinophil accumulation in the rat pleural cavity were studied using pleurisy induced by compound 48/80, a standard mast-cell-degranulating agent. Twenty-four hours after the %%%intrathoracic%%% injection of compound 48/80, (1-50 .mu.g/cavity), a dose-dependent eosinophil enrichment of the exudate was noted, concomitantly with a drastic reduction in the total number of undamaged mast cells recovered from the pleural washing. At 24

h, neutrophil counts were not modified, and the number of mononuclear cells was increased, but only at the highest dose of compound 48/80. The temporal analysis showed that mast cell degranulation, exudation and neutrophil infiltration were maximal at the interval of 1-6 h after compound 48/80 (25 :mu.g/cavity), whereas eosinophil accumulation peaked within 24 h, persisting elevated at least until 96 h. Since compound 48/80 was itself unable to induce eosinophil migration in vitro, attempts were made to investigate the potential involvement of recognized eosinophil chemo-attractants, such as histamine, %%%leukotriene%%% B4 (LTB4) and platelet-activating factor (PAF-acether). The intraperitoneal pretreatment with either cyproheptadine (2 mg/kg), meclizine (40 mg/kg), BW755C (25 mg/kg) or with the PAF-acether receptor antagonist WEB 2086 (20 mg/kg) had no effect on the eosinophil recruitment induced by compound 48/80 (25 .mu.g/cavity). However, the treatment with the corticosteroid dexamethasone or the local inhibition of protein biosynthesis with cycloheximide (0.04-200 nmol/cavity) blocked the eosinophil pleural accumulation, but not the mast cell degranulation induced by compound 48/80. Our findings indicate that the pleural eosinophil accumulation induced by compound 48/80 is sensitive to dexamethasone, requires local protein biosynthesis and is independent of histamine, LTB4 and PAF-acether.

16/7/4
DIALOG(R)File 5:Biosis Previews(R)

06251979 BIOSIS NO.: 000086086162
NEUTROPHILS IN REEXPANSION PULMONARY EDEMA
AUTHOR: JACKSON R M; VEAL C F; ALEXANDER C B; BRANNEN A L; FULMER J D
AUTHOR ADDRESS: BIRMINGHAM VETERANS ADM. MED. CENT., BIRMINGHAM 35233.
JOURNAL: J APPL PHYSIOL 65 (1). 1988. 228-234. 1988
FULL JOURNAL NAME: Journal of Applied Physiology
CODEN: JAPHE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: This study investigated the possible contribution of neutrophils to development of reexpansion pulmonary edema (RPE) in rabbits. Rabbits' right lungs were collapsed for 7 days and then reexpanded with negative %%%intrathoracic%%% pressure for 2 h before study, a model that creates unilateral edema in the reexpanded lungs but not in contralateral left lungs. Two hours after lung reexpansion, significant increases in lavage albumin concentration (17-fold), percent neutrophils (14-fold), and total number of neutrophils (7-fold) recovered occurred in the reexpanded lung but not in the left. After 2 h of reexpansion increased %%%leukotriene%%% B4 was detected in lavage supernatant from right lungs (335 .+. 33 pg/ml) compared with the left (110 .+. 12 pg/mg, P<0.01), and right lung lavage acid phosphatase activity similarly increased (6.67 .+. 0.35 U/I) compared with left (4.73 .+. 0.60 U/I, P<0.05). Neutropenia induced by nitrogen mustard (17 .+. 14> neutrophils/.mu.l) did not prevent RPE, because reexpanded lungs from six neutropenic rabbits were edematous (wet-to-dry lung weight ratio 6.34 .+. 0.43) compared with their contralateral lungs (4.97 .+. 0.04, P <0.01). An elevated albumin concentration in reexpanded lung lavage from neutropenic rabbits (8-fold) confirmed an increase in permeability. Neutrophil depletion before reexpansion did not prevent unilateral edema, although neutrophils were absent from lung sections and alveolar lavage fluid from neutropenic rabbits.

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? s s15 and administration
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? s s17 and thoracic
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18/7/1
DIALOG(R)File 5:Biosis Previews(R)

06731111 BIOSIS NO.: 000088040538
EXPERIMENTAL STUDIES ON MECHANISMS AND PREVENTION OF RADIATION PNEUMONITIS
AUTHOR: HASHIMURA T; KONO M; IMAJO Y
AUTHOR ADDRESS: DEP. RADIOL., KOBE UNIV. SCH. MED.
JOURNAL: NIPPON ACTA RADIOL 49 (3). 1989. 335-343. 1989
FULL JOURNAL NAME: Nippon Acta Radiologica
CODEN: NHGZA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Radiation pneumonitis are well recognized as complications of radiotherapy for the %%%thoracic%%% malignancies. However, the pathogenesis of radiation pneumonitis has been poorly understood and prevention of it has not been developed. In this study, to define the mechanisms of radiation pneumonitis biologically, we measured lipid peroxides, the activities of glutathione peroxidase (GSH pex.), %%%leukotriene%%% C4 and D4 (LTC4 and LTD4) in the irradiated lungs of mice. Eight weeks old female ICR mice were sacrificed at various time periods (immediately after to 5 days) following the 10 Gy whole-body irradiation with 60Co gamma rays. The lipid peroxides and the activities of GSH pex. increased immediately after the irradiation, but returned to the control level 1 hour after the irradiation. And then, the lipid peroxides also increased from 1 day after the irradiation, while the activities of GSH pex. decreased below the control level. LTC4 and LTD4 in the irradiated lungs of mice were also significantly higher than those of non-irradiated controls. Furthermore, we investigated effects of Coenzyme Q10 and Azelastine for the prevention of radiation pneumonitis. Lungs of ICR mice after 10 Gy whole-thorax irradiation treated with those drugs were compared with the control lungs pathologically. Intraperitoneal %%%administration%%% of those drugs decreased the damages for endothelium, such as vacuole formation and stripping off the basement membrane which were recognized by electron microscope. Based on these results, it was strongly suggested that initial damage of irradiated lungs might be induced by lipid peroxides and leukotriens, and that Coenzyme Q10 and Azelastine could reduce radiation pneumonitis.

18/7/2
DIALOG(R)File 5:Biosis Previews(R)

05556399 BIOSIS NO.: 000083029539
PHARMACOLOGICAL MODULATION OF THE EFFECTS OF N FORMYL-L-METHIONYL-L-LEUCYL-L-PHENYLALANINE IN GUINEA-PIGS INVOLVEMENT OF THE ARACHIDONIC-ACID CASCADE
AUTHOR: BOUKILI M A; BUREAU M; LAGENTE V; LEFORT J; LELLOUCH-TUBIANA A; MALANCHERE E; VARGAFTIG B B
AUTHOR ADDRESS: UNITE ASSOCIEE INSTITUT PASTEUR/INSERM NO. 285, DEPARTEMENT DE PHYSIOPATHOLOGIE EXPERIMENTALE, INSTITUT PASTEUR, 28 RUE DU DR ROUX, PARIS 75015, FRANCE.
JOURNAL: BR J PHARMACOL 89 (2). 1986. 349-360. 1986
FULL JOURNAL NAME: British Journal of Pharmacology
CODEN: BJPCB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: 1 The intravenous %%%administration%%% of the chemotactic and secretagogue peptide N-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP; 0.3-30 .mu.g kg-1) to the guinea-pig induces bronchoconstriction and dose-dependent leukopenia accompanied by mild thrombocytopenia. No electron microscopic evidence of platelet aggregation in lungs or significant accumulation of 111In-labelled platelets in the %%%thoracic%%% region at the height of bronchoconstriction was noted. 2 Bronchoconstriction and leukopenia induced by FMLP were not affected by prostacyclin, by platelet depletion, by the platelet-activating factor (Paf-acether) antagonist BN 52021 or by the histamine H1-antagonist mepyramine. Bronchoconstriction, but not leukopenia, was inhibited by aspirin, whereas the peptido-%%%leukotriene%%% antagonist compound FPL 55712 and the cyclo-oxygenase lipoxygenase inhibitor indomethacin reduced

bronchoconstriction to a limited extent only. The mixed cyclo-oxygenase/lipoxygenase inhibitor compound BW 755C was very effective in blocking bronchoconstriction by the highest dose of FMLP used, but failed to interfere with leukopenia. 3 FMLP-induced dose-dependent contraction of parenchymal lung strips was accompanied by the formation of immuno-reactive thromboxane B2 in amounts markedly less than those formed from exogenous arachidonic acid at concentration equieffective in inducing contractions. 4 FMLP-induced contractions of the guinea-pig lung strip were not modified by mepyramine nor by FPL 55712. They were reduced by indomethacin and aspirin and an even greater reduction was obtained with aspirin used in combination with FPL 55712, BW 755C suppressed the effects of all the concentrations of FMLP tested, whereas tert-butyloxy-carbonyl-L-methionyl-L-leucyl-L-phenylalanine, a chemical analogue of FMLP, displaced the concentration-response curve to the right, without reducing the maximal contraction obtained. 5 The present results indicate that: (a) bronchoconstriction by FMLP is not due to platelet activation, to cyclo-oxygenase-dependent mechanisms or to peptido-%%%leukotriene%%% formation. The inhibitory effect of aspirin and BW 755C involves a property other than cyclo-oxygenase inhibition, which is not shared by indomethacin. (b) The contractile effects of FMLP on parenchymal lung strips follow an interaction with specific receptor sites, as shown by the effectiveness of tert-butyloxy-carbonyl-L-methionyl-L-leucyl-L-phenylalanine, and involves the combined effects of cyclo-oxygenase and lipoxygenase metabolites.

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S6          7   S4 AND S5
S7       1220   BRONCHOSCOPE
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S10         0   ENDOTRACHEAL AND S4
S11       129   INTUBATE
S12         0   S11 AND LEUKOTRIENE
S13         1   ENTUBATE
S14      3496   INTRATHORACIC
S15     14826   LEUKOTRIENE
S16         4   S14 AND S15
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S18         2   S17 AND THORACIC
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09/291656

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(c) 2003 BIOSIS

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	1311	BRONCHOSCOPE
S1	8	LEUKOTRIENE AND BRONCHOSCOPE

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1/7/1
DIALOG(R)File 5:Biosis Previews(R)
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13715059 BIOSIS NO.: 200200343880
Inflammatory mediators in CF patients.
BOOK TITLE: Methods in Molecular Medicine Cystic fibrosis methods and protocols
AUTHOR: Hilliard Jay B(a); Konstan Michael W; Davis Pamela B
BOOK AUTHOR/EDITOR: Skach William R: Ed
AUTHOR ADDRESS: (a)Department of Pediatrics, Rainbow Babies and Children's Hospital, Case Western Reserve University School of Medicine, Cleveland, OH**USA
JOURNAL: Methods in Molecular Medicine 70p409-431 2002
MEDIUM: print
BOOK PUBLISHER: Humana Press Inc., 999 Riverview Drive, Suite 208, Totowa, NJ, 07512, USA
ISBN: 0-89603-897-1 (cloth)
DOCUMENT TYPE: Book
RECORD TYPE: Citation
LANGUAGE: English

1/7/2
DIALOG(R)File 5:Biosis Previews(R)
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12803233 BIOSIS NO.: 200100010382
Eicosanoid and muscarinic receptor blockade abolishes hyperventilation-induced bronchoconstriction.
AUTHOR: Freed Arthur N(a); McCulloch Sharron; Wang Yongqiang
AUTHOR ADDRESS: (a)School of Hygiene and Public Health, Johns Hopkins Univ., 615 North Wolfe St., Div., Rm. 7006, Baltimore, MD, 21205**USA
JOURNAL: Journal of Applied Physiology 89 (5):p1949-1955 November, 2000
MEDIUM: print
ISSN: 8750-7587
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: This study was designed to test the hypothesis that hyperventilation-induced bronchoconstriction (HIB) results from the combined effects of prostanoid and %%%leukotriene%%% metabolism. A %%%bronchoscope%%% was used in anesthetized dogs to record peripheral airway resistance and HIB before and after combined treatment with inhibitors of cyclooxygenase (indomethacin) and 5-lipoxygenase (MK-0591). Bronchoalveolar lavage fluid (BALF) cells and mediators from hyperventilated and control airways were also measured. Pretreatment with MK-0591 and indomethacin significantly attenuated, but did not abolish, HIB. However, addition of atropine nearly eliminated the residual response. Blockade of eicosanoid metabolism markedly reduced the concentrations of eicosanoids recovered in BALF after hyperventilation. Positive correlations between post-hyperventilation BALF prostanoid and epithelial cell concentrations are suggestive of mucosal injury-induced mediator production and release. We conclude that HIB is prevented in the presence of eicosanoid and muscarinic-receptor blockade and that both classes of eicosanoids contribute similarly to the development of HIB.

12578714 BIOSIS NO.: 200000332216
Heparin inhibits eicosanoid metabolism and hyperventilation-induced bronchoconstriction in dogs.
AUTHOR: Suzuki Ryoichi; Freed Arthur N(a)
AUTHOR ADDRESS: (a)Division of Physiology, Johns Hopkins University, 615 North Wolfe Street, 7006 SHPH, Baltimore, MD, 21205**USA
JOURNAL: American Journal of Respiratory and Critical Care Medicine 161 (6):p1850-1854 June, 2000
MEDIUM: print
ISSN: 1073-449X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Inhalation of heparin, an anticoagulant, attenuates exercise-induced asthma (EIA) in human subjects. The purpose of this study was to determine if heparin inhibits hyperventilation-induced bronchoconstriction (HIB) in a canine model of EIA, and if its mode of action involves the inhibition of eicosanoid mediator production and release. We used a wedged %%%bronchoscope%%% technique to measure baseline peripheral airway resistance (Rp). We then performed either a 2-min or 5-min dry air challenge (DAC) by temporarily increasing from 200 to 2,000 ml/min the flow of 5% CO2 in air used to ventilate a wedged sublobar segment. We compared HIB before and 60 min after aerosol treatment with either bacteriostatic water (BW) or heparin. We found that (1) heparin had no effect on baseline Rp, (2) BW did not alter the response to DAC, and (3) heparin reduced HIB by apprx 50-60%. On the

basis of bronchoalveolar lavage fluid (BALF) cell analysis, heparin and BW caused acute infiltration of macrophages and eosinophils, and heparin increased the number of erythrocytes recovered immediately after DAC. Despite these acute inflammatory effects initiated prior to DAC, BALF mediator analyses revealed that pretreatment with heparin either attenuated or abolished hyperventilation-induced %%%leukotriene%%%, prostaglandin, and thromboxane release. Thus, our data provide direct evidence that inhaled heparin inhibits eicosanoid mediator production and release caused by hyperventilation with dry air, and significantly attenuates HIB.

1/7/4
DIALOG(R)File 5:Biosis Previews(R)

07253867 BIOSIS NO.: 000090033743
DRY AIR-INDUCED LATE PHASE RESPONSES IN THE CANINE LUNG PERIPHERY
AUTHOR: FREED A N; ADKINSON N F JR
AUTHOR ADDRESS: DIV. OF PHYSIOL., 7006 HYGIENE, JOHNS HOPKINS UNIV., 615 NORTH WOLFE ST., BALTIMORE, MARYLAND 21205, USA.
JOURNAL: EUR RESPIR J 3 (4). 1990. 434-440. 1990
FULL JOURNAL NAME: European Respiratory Journal
CODEN: ERJOE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Although controversial, late phase responses in asthmatic subjects have been reported several hours after exercise. We previously showed that exposure to dry air increases collateral system resistance (Rcs) in the canine lung periphery, and produces acute airway responses analogous to those that characterize human exercise-induced asthma. We used a dual wedged %%%bronchoscope%%% technique in anaesthetized male mongrel dogs to monitor Rcs in: 1) control segments continuously exposed to 200 ml.cntdot.min-1 of 5% CO2 in air and 2) dry air challenged segments exposed to 2000 ml.cntdot.min-1 5% CO2 for 5 min. We examined Rcs at 5 min .apprx.5 h post-challenge in an attempt to document late phase airway obstruction. Five min after dry air challenge Rcs initially increased 114.+.SE 22%; contralateral control segments remained unchanged (n=9). Five hour post-challenge, Rcs in dry air segments was elevated 81.+.20% above pre-challenge baseline ($p<0.01$); contralateral control segments did not change significantly over the 5 h period. cell profile analyses of lavage samples at 5 hours revealed that neutrophils and eosinophils were significantly increased ($p<0.03$) in dry air challenged segments when compared to controls. %%%Leukotriene%%% C4/D4 concentration in lavage was correlated ($p<0.02$) with neutrophil infiltration. Thus, we conclude that the canine lung periphery represents a reproducible model of a dry air-induced late phase reaction.

1/7/5
DIALOG(R)File 5:Biosis Previews(R)

07165781 BIOSIS NO.: 000089032424
EFFECTS OF %%%LEUKOTRIENE%%% B-4 IN THE HUMAN LUNG RECRUITMENT OF NEUTROPHILS INTO THE ALVEOLAR SPACES WITHOUT A CHANGE IN PROTEIN PERMEABILITY
AUTHOR: MARTIN T R; PISTORESE B P; CHI E Y; GOODMAN R B; MATTHAY M A
AUTHOR ADDRESS: PULMONARY AND CRITICAL CARE MED., SEATTLE VETERANS ADMINISTRATION MED. CENT., 1660 S. COLUMBIAN WAY, SEATTLE, WASH. 98108.
JOURNAL: J CLIN INVEST 84 (5). 1989. 1609-1619. 1989
FULL JOURNAL NAME: Journal of Clinical Investigation
CODEN: JCINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Leukotriene%%% B4 (LTB4) is a major product of human alveolar macrophages and has potent chemotactic activity for neutrophils (PMN) in vitro. To evaluate the effects of LTB4 in the normal human lung, we instilled LTB4 (5 .times. 10-7M, 10 ml) into a subsegment of the right middle lobe and 0.9% NaCl (10 ml) into a subsegment of the lingula using a fiberoptic %%%bronchoscope%%% in 12 healthy human volunteers. 4 h later, we performed bronchoalveolar larvage of the same subsegments. Compared with the NaCl instillation, LTB4 caused a large increase in lavage total cells (NaCl = 6.8 .+. 1.0 .times. 106 vs. LTB4 = 26.4 .+. 5.0 .times. 106, P < 0.001), most of which were PMN (NaCl = 12.2 .+. 4.6% vs. LTB4 = 55.7 .+. 6.0%, P < 0.001). In contrast, there was only a small increase in lavage total protein, and the lavage total protein correlated weakly with lavage total cells and PMN. The production of superoxide anion by the lavage PMN in response to phorbol myristate acetate was similar to that of peripheral blood PMN. The migration of lavage PMN was normal toward the chemotactic peptide FMLP, but reduced toward LTB4 and zymosan-activated human serum. Morphometric analysis using transmission electron microscopy indicated a selective loss of small granules in the lung neutrophils as compared with peripheral blood neutrophils. The data indicate that in the normal human lung, LTB4 can recruit active PMN into the airspaces without causing a significant change in the protein permeability of the epithelial barrier.

1/7/6
DIALOG(R)File 5:Biosis Previews(R)

06722881 BIOSIS NO.: 000088032307
USE OF SEGMENTAL AIRWAY LAVAGE TO OBTAIN RELEVANT MEDIATORS FROM THE LUNGS
OF ASTHMATIC AND CONTROL SUBJECTS
AUTHOR: ZEHR B B; CASALE T B; WOOD D; FLOERCHINGER C; RICHERSON H B; HUNNINGHAKE G W
AUTHOR ADDRESS: DEP. INTERNAL MED. C33-G, CH, UNIV. IOWA COLL. MED., IOWA CITY, IOWA 52242.
JOURNAL: CHEST 95 (5). 1989. 1059-1063. 1989

FULL JOURNAL NAME: Chest
CODEN: CHETB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Studies have demonstrated that increased amounts of histamine in the airways of asthmatic patients are associated with increased airway reactivity. However, using routine bronchoalveolar lavage (BAL), histamine can be detected in only a portion of asthmatic subjects and a minority of control populations. To obtain relevant mediators from the airways in higher concentrations by avoiding the dilution inherent with a standard BAL, a technique was developed to lavage isolated airway segments of the human lung that employed a double-lumen %%%bronchoscope%%% and a balloon-tipped catheter. Lavage fluid obtained by this method yielded significantly higher concentrations of histamine than that obtained with routine BAL (asthmatic subjects, 2,403 .+. 633 pg/ml vs 188 .+. 42 pg/ml; rhinitis subjects, 533 .+. 187 pg/ml vs 113 .+. 53 pg/ml; normal subjects, 174 .+. 63 pg/ml vs 11 .+. 11 pg/ml). Similar findings were also noted for prostaglandin D2 (PGD2). Segmental airway lavage also resulted in higher lavage fluid concentrations of LTB4 than routine BAL. Segmental airway lavage should help in studying the relationship of mast cell degranulation to airways reactivity in both asthmatic and other study populations.

1/7/7
DIALOG(R)File 5:Biosis Previews(R)

06285324 BIOSIS NO.: 000086119507
DIFFERENTIAL RESPONSES OF TISSUE VISCANCE AND COLLATERAL RESISTANCE TO HISTAMINE AND %%%LEUKOTRIENE%%% C-4
AUTHOR: LUDWIG M S; SHORE S A; FREDBERG J J; DRAZEN J M
AUTHOR ADDRESS: DEP. MED., BRIGHAM AND WOMEN'S HOSP., HARVARD MED. SCH.,
HARVARD SCH. PUBLIC HEALTH, BOSTON, MASS. 02115.
JOURNAL: J APPL PHYSIOL 65 (3). 1988. 1424-1429. 1988
FULL JOURNAL NAME: Journal of Applied Physiology
CODEN: JAPHE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alterations in tissue viscance (Vti) and collateral resistance (Rcoll) are both used as indexes of peripheral lung responses. However, it is not known whether the two responses reflect the effects of activation of the same contractile elements. We measured differential responses in Vti and Rcoll to histamine and %%%leukotriene%%% (LT) C4 to determine whether each evoked a similar pattern of response. Using the wedged %%%bronchoscope%%% constant-flow technique, we measured Rcoll in lobar segments of anesthetized, paralyzed, open-chest, mechanically ventilated mongrel dogs. In addition, we measured (with an alveolar capsule) alveolar pressure (PA) within the segment under study. This

allowed us to calculate Vti, the component of the PA change in phase with segment flow. Rcoll and Vti measurements were obtained under base-line conditions and after local delivery of aerosols generated from histamine and LTC4. In five out of five lobes studied with both histamine and LTC4, the fractional Rcoll response to histamine was greater than the fractional Rcoll response to LTC4. In contrast, in four out of five lobes examined, the fractional increase in Vti accompanying the histamine response was less than the fractional increase in Vti accompanying LTC4 administration. These data suggest that anatomically distinct contractile elements influence Vti and Rcoll insofar as LTC4 and histamine evoke quantitatively different changes in these two indexes of peripheral lung responses.

1/7/8
DIALOG(R)File 5:Biosis Previews(R)

05429389 BIOSIS NO.: 000033030236
DIFFERENTIAL RESPONSES OF COLLATERAL RESISTANCE AND TISSUE VISCANCE TO HISTAMINE AND %%%LEUKOTRIENE%%% C-4
AUTHOR: LUDWIG M; SHORE S; FREDBERG J; DRAZEN J M
AUTHOR ADDRESS: HARVARD SCH. PUBLIC HEALTH, BRIGHAM AND WOMEN'S HOSP.,
BOSTON, MASS. 02115.
JOURNAL: JOINT ANNUAL MEETING OF THE AMERICAN LUNG ASSOCIATION AND THE
AMERICAN THORACIC SOCIETY, NEW ORLEANS, LOUISIANA, USA, MAY 10-13, 1987. AM
REV RESPIR DIS 135 (4 PART 2). 1987. A92. 1987
CODEN: ARDSB
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
? s leukotriene and endotrach?
15483 LEUKOTRIENE
5747 ENDOTRACH?
S2 7 LEUKOTRIENE AND ENDOTRACH?
? t s2/7/1-7

2/7/1
DIALOG(R)File 5:Biosis Previews(R)

07822824 BIOSIS NO.: 000092104010
GRANULOCYTE CHEMOTAXIS IN THE CANINE TRACHEA INHIBITION BY LIPID MEDIATOR
ANTAGONISTS AND SYSTEMIC INHIBITORS
AUTHOR: JOHNSON H G; MCNEE M L
AUTHOR ADDRESS: HYPERSENSITIVITY DISEASE RES., UPJOHN CO., 301 HENRIETTA ST., KALAMAZOO, MICH. 49007, USA.
JOURNAL: AGENTS ACTIONS 33 (3-4). 1991. 260-271. 1991

FULL JOURNAL NAME: Agents and Actions
CODEN: AGACB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Inflammation of the airways contributes to the multicomponent disease known as asthma. The primary cells that infiltrate the airways in response to antigen exposure are PMNs and eosinophils, cells that can release cellular components, and damage the airways. We adapted a double-balloon %%%endotracheal%%% tube to study the cellular response to three de novo synthesized lipid mediators (LTB4, PAF-acether and 15 HETE) found in respiratory fluids following antigen exposure. In random repeat challenges in groups of 7 dogs using mongrel dogs at 240 min following exposure to 10-6 M agonists, the PMN content of the perfused fluid was 870 .+. 240, 1632 .+. 883, 515 .+. 395, and 1575 .+. 214 cells/ml/5 high power fields for vehicle, LTB4, PAF, and 15 HETE respectively. Eosinophils that infiltrated the lumen at 240 min 162 .+. 23, 608 .+. 287, 502 .+. 23, 115 .+. 14 cells/ml/5 HPF for vehicle, LTB4, PAF, and 15 HETE respectively. Thus LTB4 and PAF-acether significantly ($p < 0.05$) increased eosinophils, and LTB4 and 15 HETE increased PMNs ($p < 0.05$). After determining the agonist response for the 3 agonists we included 2 specific antagonists in the perfusate. The LTB4 antagonist U-75,302 10-5 M, and the PAF antagonist L 652,731 10-5 M in chambers containing LTB4 and PAF-acether respectively blocked significantly the influx of PMNs and eosinophils compared to vehicle ($P < 0.01$). Methylprednisolone 5 mg/kg i.m. - 18 hrs blocked eosinophilia to PAF and LTB4. Oral U-78,517F a Trolox amine lazaroid, active as an inhibitor of lipid peroxidation, 30 mg/kg - 18 hrs significantly blocked eosinophilia to PAF-acether and LTB4 directed chemotaxis compared to vehicle ($p < 0.05$) but not 15 HETE. Specificity was shown for each antagonist since the PAF and LTB4 antagonists did not block the opposite agonist. Use of this novel in vivo chemotaxis model allows the additional advantage of studying chemotaxis in living tissue.

2/7/2
DIALOG(R)File 5:Biosis Previews(R)

07697092 BIOSIS NO.: 000041030048
%%%LEUKOTRIENE%%% GENERATION AND CELL ACCUMULATION IN LUNG INJURY INDUCED
BY %%%ENDOTRACHEAL%%% SILICA INSTILLATION
AUTHOR: ISHIHARA Y; KAGAWA J
AUTHOR ADDRESS: TOKYO WOMEN'S MED. COLL., TOKYO, JPN.
JOURNAL: INTERNATIONAL CONFERENCE OF THE AMERICAN LUNG ASSOCIATION AND THE
AMERICAN THORACIC SOCIETY, ANAHEIM, CALIFORNIA, USA, MAY 12-15, 1991. AM REV RESPIR DIS 143 (4 PART 2). 1991. A491. 1991
CODEN: ARDSB
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation

LANGUAGE: ENGLISH

2/7/3
DIALOG(R)File 5:Biosis Previews(R)

07325646 BIOSIS NO.: 000090105547
ROLE OF %%%LEUKOTRIENE%%% D-4 IN THE EARLY AND LATE PULMONARY RESPONSES OF
RATS TO ALLERGEN CHALLENGE
AUTHOR: SAPIENZA S; EIDELMAN D H; RENZI P M; MARTIN J G
AUTHOR ADDRESS: MEAKINS-CHRISTIE LAB., MCGILL UNIV., 3626 ST. URBAIN ST., MONTREAL, QUEBEC, CAN. H2X 2P2.
JOURNAL: AM REV RESPIR DIS 142 (2). 1990. 353-358. 1990
FULL JOURNAL NAME: American Review of Respiratory Disease
CODEN: ARDSB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: To examine the role of %%%leukotriene%%% D4 (LTD4) in early and late pulmonary responses to antigen, we evaluated the effects of two LTD4 antagonists, MK-571 and FPL-57231, on the changes in pulmonary resistance (RL) in the 8-h period following antigen challenge of allergic rats. A total of 69 rats, aged 6 to 8 wk, were sensitized to subcutaneous ovalbumin (OA, 1 mg) and intraperitoneal BordeteHa pertussis vaccine (6 .times. 109 bacilli). At 14 days after sensitization, rats were anesthetized with intraperitoneal urethane (1.1 g/kg) and intubated %%%endotracheally%%%. Aerosols of OA (5% wt/vol in saline for 5 min) were administered to 24 control rats, to 11 rats that were pretreated with aerosolized FPL-57231, and to 8 rats that were pretreated with MK-571; 6 rats also received MK-571 at 2 h after OA. A control group of 13 rats was challenged with aerosois of saline. We defined an early response (ER) as an increase in RL to at least 150% of the postsaline value occurring within 1 h after OA challenge. A late response (LR) was defined as a value of RL exceeding the mean plus 2 SD of all values of RL from 75 min to 8 h after OA challenge and lasting at least 30 min. An ER was observed in 17 of 24 controls rats, in 8 of 11 FPL-57231-pretreated rats, and in 3 of 8 MK-571-pretreated rats (not significant). The magnitude and duration of the ER were significantly reduced by MK-571, whereas only the duration was affected by FPL-57231. An LR was observed in 11 of 24 control rats. Rats pretreated with FPL-57231 and MK-571 did not show any significant LR. We conclude that LTD4 is an important mediator of the ER and LR in the Brown-Norway rat.

2/7/4
DIALOG(R)File 5:Biosis Previews(R)

06787213 BIOSIS NO.: 000088096650

CHEMOTACTIC FACTOR GENERATION AND CELL ACCUMULATION IN ACUTE LUNG INJURY
INDUCED BY %%%ENDOTRACHEAL%%% ACID INSTILLATION
AUTHOR: ISHII Y; KOBAYASHI J; KITAMURA S
AUTHOR ADDRESS: DEP. PULMONARY MED., JICHI MED. SCH., MINAMI-KAWACHI, TOCHIGI, 329-04, JPN.
JOURNAL: PROSTAGLANDINS LEUKOTRIENES ESSENT FATTY ACIDS 37 (1). 1989. 65-70. 1989
FULL JOURNAL NAME: Prostaglandins Leukotrienes and Essential Fatty Acids
CODEN: PLEAE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We studied the time course of chemotactic factor generation and inflammatory cell accumulation in the rabbit aspiration pneumonia model. Two major potent chemotactic factors, %%%leukotriene%%% B4 (LTB4) and C5a, in bronchoalveolar lavage fluid (BALF) were measured by radioimmunoassay, and cell analysis was also done. The level of LTB4 increased only in the early phase (2-6 h) after %%%endotracheal%%% acid instillation. The level of C5a increased gradually almost in parallel with the total protein level in BALF, and reached a maximum at 24 h. Neutrophil accumulation occurred early and reached a maximum at 24 h. In contrast, the number of alveolar macrophages increased from days 1 to 7. These findings suggest that the increases in LTB4 and C5a are responsible for accumulation of neutrophils and that C5a may be an important chemotactic factor for alveolar macrophage.

2/7/5

06193086 BIOSIS NO.: 000086027268
AN IN-VIVO CHEMOTAXIS ASSAY IN THE DOG TRACHEA EVIDENCE FOR CHEMOTACTIC
ACTIVITY OF 8 15 DIHETE
AUTHOR: KIRSCH C M; SIGAL E; DJOKI T D; GRAF P D; NADEL J A
AUTHOR ADDRESS: SANTA CLARA VALLEY MED. CENT., 751 S. BASCOM AVE., SAN JOSE, CA 95128.
JOURNAL: J APPL PHYSIOL 64 (5). 1988. 1792-1795. 1988
FULL JOURNAL NAME: Journal of Applied Physiology
CODEN: JAPHE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We describe a new in vivo chemotaxis assay in the dog trachea using a double-balloon %%%endotracheal%%% catheter. When inflated, the two balloons isolate a segment of trachea, which is perfused through Silastic tubes using a peristaltic pump. After instilling a chemotactic agent, the perfusate is sampled periodically to permit characterization of the chemotactic response. We anesthetized four mongrel dogs and ventilated them mechanically through the double-balloon catheter. Two

mediators, %%%leukotriene%%% B4 (LTB4) and 8S,15S-dihydroxyeicosatetraenoic acid (8,15-diHETE) were tested in each dog by perfusing the trachea with each mediator in Hanks balanced salt solution (HBSS) containing ethanol and antibiotics. Aliquots were removed for differential cell counts at fixed time intervals over a 4-period. Control experiments performed in each dog with the identical concentrations of ethanol and antibiotics in HBSS showed no cellular response before 180 min. At 240 min, the cell counts were 86 .+. 28 (SE) granulocytes/.mu.l (n = 4). In contrast, both LTB4 and 8,15-diHETE gave a significant cellular response at 120 min (309 .+. 125 and 141 .+. 4.1 granulocytes/.mu.l, respectively; P < 0.05) but did not differ significantly from each other. These results suggest that both LTB4 and 8,15-diHETE can incite inflammatory responses in the dog trachea in vivo. Furthermore, the double-balloon catheter technique promises to be a useful in vivo chemotaxis assay.

2/7/6
DIALOG(R)File 5:Biosis Previews(R)

05816131 BIOSIS NO.: 000034039280
THE CHEMOTACTIC FACTOR GENERATION AND CELL ACCUMULATION IN ACUTE LUNG
INJURY INDUCED BY %%%ENDOTRACHEAL%%% ACID INSTILLATION
AUTHOR: ISHII Y; KOBAYASHI J; SUGAMA Y; KITAMURA S
AUTHOR ADDRESS: DEP. PULMONARY MED., JICHI MED. SCH., TOCHIGI, JPN.
JOURNAL: 53RD ANNUAL SCIENTIFIC ASSEMBLY OF THE AMERICAN COLLEGE OF CHEST
PHYSICIANS, ATLANTA, GEORGIA, USA, OCTOBER 26-30, 1987. CHEST 92 (2 SUPPL.). 1987. 56S. 1987
CODEN: CHETB
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

2/7/7
DIALOG(R)File 5:Biosis Previews(R)

04685218 BIOSIS NO.: 000079098347
AIRWAY RESPONSES TO AEROSOLIZED %%%LEUKOTRIENE%%% D-4 IN NORMAL AND ASCARIS
REACTOR PRIMATES
AUTHOR: JOHNSON H G; STOUT B K
AUTHOR ADDRESS: HYPERSENSITIVITY DISEASES RESEARCH, THE UPJOHN COMPANY, 301
HENRIETTA STREET, KALAMAZOO, MICHIGAN 49001.
JOURNAL: PROSTAGLANDINS 29 (2). 1985. 313-322. 1985
FULL JOURNAL NAME: Prostaglandins
CODEN: PRGLB

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Normal and Ascaris reactor primates [rhesus monkey] were compared for their bronchial pulmonary response to aerosolized %%%leukotriene%%% D4 (LTD4). When 10 .mu.g/ml LTD4 was aerosolized (total amount delivered to %%%endotracheal%%% tube was 1.0 .mu.g) into the lungs of 6 normal primates, a small increase in total lung resistance (RL) was noted (4.4 .+. 4.5% increase, in 19 separate challenges). A larger effect was seen in compliance (27.6 .+. 15.% decrease, n = 19). Ascaris reactors (n = 4) demonstrated a larger RL effect than normals with almost an identical Cdyn [dependence of lung compliance] change (RL 36.1 .+. 27.7% increase, Cdyn 32.8 .+. 18.8% decrease n = 12). When the pharmacological blockers diphenhydramine, 0.5 mg/kg and atropine, 0.5 mg/kg were administered i.v. separately before LTD4 challenge, significant antagonist activity was seen. Diphenhydramine inhibited the LTD4 response in normal primates (RL 64.2 .+. 44.3% and Cydn 50.5 .+. 40.9% n = 6) and in reactors (RL 47.8 .+. 43.1% and Cdyn 19.2 .+. 20.8% n = 4). Atropine inhibited normals (RL 100% and Cdyn 73.1 .+. 32.7% n = 2) and reactors (RL 96.3 .+. 7.7 and Cdyn 47.4 .+. 35.1% n = 3). Apparently, the LTD agonist action is partially mediated through histamine, primarily acting on lung resistance (large airways) and, in addition, may have a reflex atropine-sensitive component. The difference between the response of normal and reactor primates to LTD4 is primarily a histamine-mediated large airway response.
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Set	Items	Description
S1	8	LEUKOTRIENE AND BRONCHOSCOPE
S2	7	LEUKOTRIENE AND ENDOTRACH?

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01jul03 09:47:08 User217744 Session D817.3
$2.71 0.484 DialUnits File5
$26.25 15 Type(s) in Format 7
$26.25 15 Types
$28.96 Estimated cost File5
$0.92 TELNET
$29.88 Estimated cost this search
$29.89 Estimated total session cost 0.732 DialUnits
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